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13. Abstract *(Maximum 200 Words) (abstract should contain no proprietary or confidential information)*

It has been shown that the development of certain types of cancer can be hormone dependent. Estrogens, such as estradiol, have the ability to bind as ligands to the estrogen receptor in the first of many steps which could result in the activation or repression of genes critical in the mechanism of tumor growth. The principle objective of this proposal is to relate known biological reactions to physical properties such as point charges of atoms and the electrostatic potential.

We are obtaining information about these electronic properties of estrogen derivatives from experimental determination of their electron density using high quality single crystal X-ray crystallography. During the past year, the focus was in completing Task 3, analysis of charge density data sets, for three systems (17β-estradiol•½MeOH, 17α estradiol•½H_2O, and 17α-estradiol•urea). Data integration techniques have been refined to improve overall data quality and consistency. Topological analysis has been completed, while analysis of the electrostatic potential is nearly complete. Initial comparisons have yielded some expected and unexpected results. These will be discussed in the body of the report. Continued effort must be made to obtain more quality data of different systems to increase the amount of data we have to reference to.

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Table of Contents

Introduction

It has been shown that the development of certain types of cancer can be hormone dependent. Estrogens, such as estradiol, have the ability to bind as ligands to the estrogen receptor in the first of many steps which could result in the activation (agonistic effect) or repression (antagonistic effect) of genes critical in the mechanism of tumor growth. It is the object of this study to relate physical and chemical properties of estrogen derivatives to certain observed biological functions. It is hoped that detailed analysis of X-ray crystallographic data will provide important information to assist in the development of therapeutic drugs. My role is the experimental determination of the electron density distribution of several estrogens as part of a larger study to investigate a wide variety of estrogens.

Body

Task 1. Preliminary studies on a series of crystals of 'A- and D-ring' estrogen derivatives.

- Develop crystallization methods for the derivatives which are not yet available as charge density quality single crystals.
  - I had previously found crystallization methods for the following compounds:
    17β-estradiol • urea
    17α-estradiol • ½ H_2O
    17β-estradiol • ½ MeOH
    17β-estradiol • ⅔ MeOH • ⅓ H_2O
    Currently the best conditions found so far involve dissolving 17β-estradiol or 17α-estradiol in "wet" methanol. Allowing the solvent to evaporate as slowly as possible (~2-4 weeks) will yield charge density quality crystals. Unfortunately, this can result in the formation of different crystal systems (such as 17β-estradiol • ½ MeOH or 17β-estradiol • ⅔ MeOH • ⅓ H_2O). "Wet" methanol is obtained by simply allowing methanol to sit for extended periods to absorb atmospheric water.

- Temperature studies on each derivative to establish tolerances and the appropriate temperatures for the measurements.
  - Several crystals were taken to the synchrotron source at Argonne National Labs in order to obtain data below liquid nitrogen temperatures. These tests were unsuccessful, we still encounter problems with crystal stability while cooling to liquid helium temperatures.

- Preliminary routine X-ray crystal structure determination on each derivative to check for composition, quality, and solvation.
  - No additional work has been done in this area in the past year.

Task 2. Electron density quality data collection on the above mentioned estrogen analogues.

- X-ray diffraction studies at liquid nitrogen temperatures on crystals that did not qualify for lower temperatures.
  - No additional work has been done in this area in the past year.

- X-ray diffraction studies at liquid helium temperatures.
  - Work has been continued to try to find a better strategy for cooling crystals down to near liquid He temperatures.

Task 3. Interpretation and analysis of nitrogen and helium temperature charge density data sets of above mentioned estrogen analogues.

- Analysis of the experimental data.

  ** Complete detailed results of the three structures are given in the appendices attached at the end of the report. They include data collection parameters, integration parameters and statistics, reflection statistics, positional and thermal parameters, bond lengths and angles, starting values for multipole refinements, final monopole and multipole populations, results from the topological analysis, as well as several diagrams of the final models.

  - It was stated in last year's report that the charge density data of the three systems collected so far had been treated and the studies had moved on to the multipole refinement. It was discovered after attempting multipole refinements of the three systems that our process for data treatment was not consistent enough to yield reliable results. The problems lie in the integration of the raw data. This required that we take a step back and reevaluate the application of the software we use.
  - Integration of the raw data involves integrating the intensity of the reflections as measured by a two-dimensional CCD detector. Several parameters must be defined to determine exactly how the software integrates the reflections. It was the combination of parameters that had to be refined. There are three parmeters which critically affect the outcome of the integration, and they are:
    - Box Size - area on 2-dimensional frame to be integrated for each reflection
    - Profile Fitting Limits – threshold for reflections which are used to determine the profiles applied in the fitting.
    - Simple Sum Perimeter Limit – Determines how far out on the reflection profile to integrate

    It was found that different detector settings, even for the same data set, require different box size parameters and profile fitting limits. The simple sum perimeter limit of 0.02 was found to be the best value for all three data sets.
  - The multipole model requires a local coordinate system be set up for every atom. The same coordinate system was applied to each structure where possible. This coordinate system is shown in detail in Appendix A starting on p. 9.
  - It was found that the starting values for the multipole model greatly influenced the path the refinement would take. It was determined that a specific set of starting

values should be applied to each structure to ensure consistency. These optimum values are shown in the appendices of the specific structures.

- 17β-estradiol • urea: As stated last year, the first data set was not usable. The second data set collected was of high quality. This allowed the multipole refinement to be completed as well as full topological analysis. Complete results are in Appendix B beginning on p. 13.
- 17β-estradiol • ½ MeOH: Despite the fact that the crystal system is P1, meaning there is no symmetry equivalent data which reduces redundancy in the data, the multipole refinement was successfully completed as well as full topological analysis. Complete results are in Appendix C beginning on p. 45.
- 17α-estradiol • ½ H_2O: The water molecule of this system lies on a 2-fold axis of rotation, meaning only half of the molecule is unique. This in itself is not a problem except that it was discovered during the multipole refinement that the hydrogen atom was very slightly disordered. The position it refined to generated a symmetry equivalent hydrogen atom which created an H – O – H bond angle of less than 90°. The thermal parameter of the hydrogen atom is twice as large as a typical hydrogen atom of the system. Due to the fact the disorder is a result of a shift on the order of 0.1 Angstroms for the hydrogen, the effect of this disorder is taken up by the large thermal parameter of the hydrogen. Unfortunately this disorder greatly effects the hydroxy atoms that are hydrogen bound to the water. This complicated the refinement significantly, however it was successfully completed as well as full topological analysis. The Complete results are in Appendix D beginning on p. 93.
- Some analysis of the electrostatic potential has been completed on the 17β-estradiol • urea and 17β-estradiol • ½ MeOH systems. Some plots can be seen in the appendices. No analysis of the electrostatic potential for the 17α-estradiol • ½ H_2O system has yet been done.

- Comparison of the results from the series of estrogen analogues.
  - Initial comparisons of the multipole models and the topological analysis have yielded expected and unexpected results. It was expected that the core structure of the estrogen molecules would remain relatively unchanged from system to system even with chemical substitutions at the activity-sensitive ends. This was found to be the case.
  - One major question that needed to be answered was could such small features as oxygen lone pair densities be determined on such large systems. If they could be determined, then you have to ask; Would they be affected by different hydrogen bonding schemes? Would the lone pair density of the oxygen's on the aromatic ring conjugate to the pi system of the aromatic ring? The answer is that we can determine features such as lone pair densities on the oxygen's (see diagrams in appendices). It was found that each oxygen atom had two lone pairs in a rough sp^3 type geometry. This demonstrates that the lone pairs are surprisingly robust in that they do not significantly change in different hydrogen bonding schemes and when the oxygen is bound to aromatic systems. This was somewhat surprising, however this type of analysis is not well represented in the literature.

- Initial tests indicate that the electrostatic potential around these oxygen's are also quite consistent, not changing significantly with different hydrogen bonding environments. This concept requires completion of the electrostatic potential calculations to be sure.

- Analyze relationship of charge density to receptor binding affinity and the chemical/biological effects as related to breast cancer.
  - This step can not be started until a sufficient amount of charge density studies have been completed successfully. Completion of these three structures, as well as structures soon to be completed by other group members, should allow this to begin in the near future.

- Final analysis and preparation of manuscripts.
  - Manuscripts have been started and will be completed as a series of papers upon completion of the electrostatic potential analysis. It is our hope that the manuscripts will be successfully submitted to the Journal of the American Chemical Society.
  - A manuscript has been submitted discussing 17β-estradiol • ⅔ MeOH • ⅓ H_2O system.

Key Research Accomplishments

- The core estrogen structure is very consistent between derivatives.
- Determination that it is possible to locate lone pair densities of oxygen's in such large systems
- Determination that the oxygen atoms of these systems are decidedly sp^3 in shape despite the fact they are bound to aromatic neighbors.
- Determination that the lone pairs appear to be unaffected by completely different hydrogen bonding environments.
- Initial suggestion that the electrostatic potential around the oxygen atoms are consistent in the face of different chemical environments.

Reportable Outcomes

- There were no reportable outcomes to present from the last year.

Conclusion

During the past year, I have made significant progress with three of the derivatives (17β-estradiol • ½ MeOH, 17α estradiol • ½ H_2O, and 17α-estradiol • urea). Initial comparisons of the results of these refinements have yielded interesting results, some expected, some not. Determining the consistency or inconsistency in the properties of the estrogen derivatives in different environments is key in understanding how they behave in the body and in the active site. The completion of these studies, along with the other derivatives being studied within the research group should begin to provide a reasonable pool of data to further enhance the preliminary findings. Continued effort must be made to analyze the electrostatic potential and determine how the charge density relates to receptor binding affinity and the chemical/biological effects as related to breast cancer. This is necessary in order for us to reach our intended goal of developing a new method of advanced drug design.

Appendix A
Coordinate System Setup

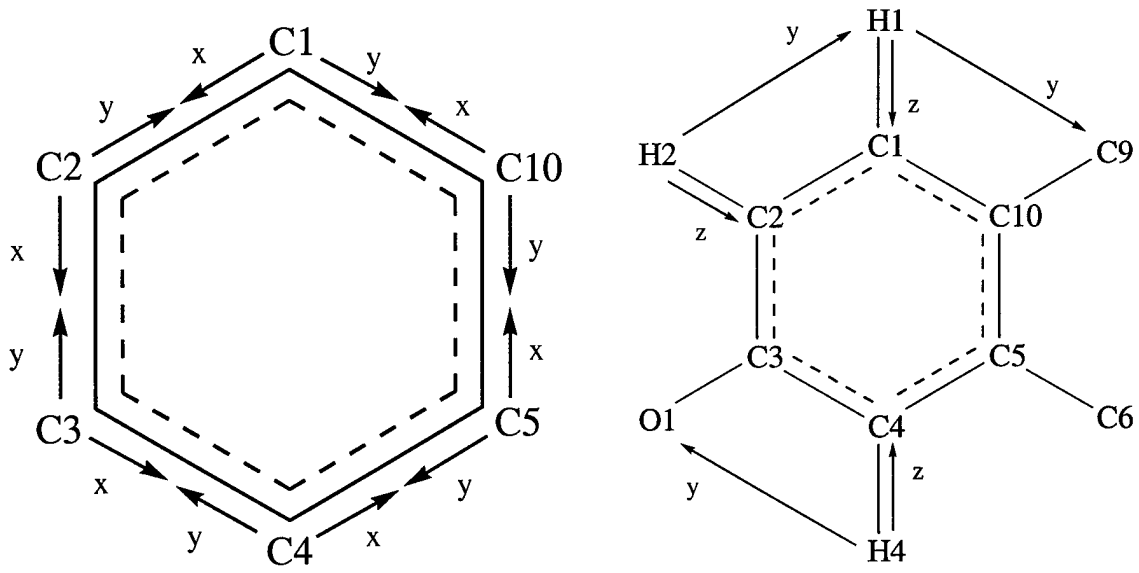

Figure A-5. Coordinate system setup for the A-ring carbon and hydrogen atoms.

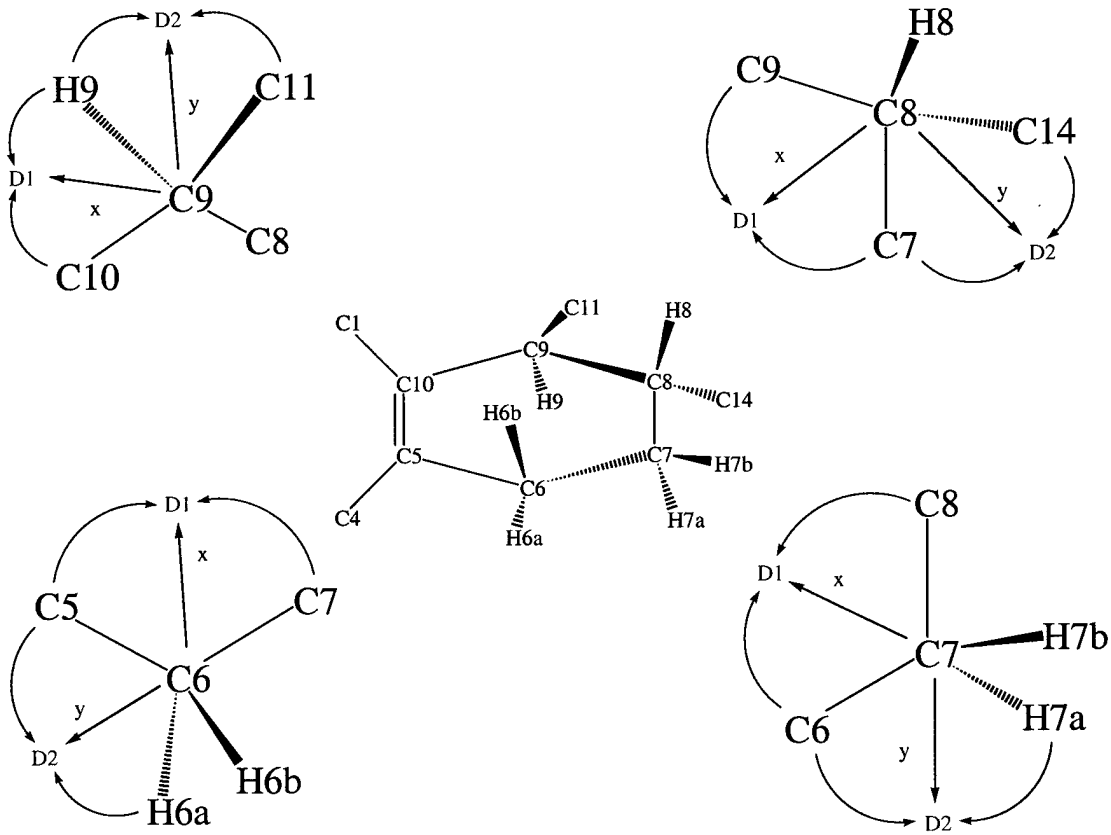

Figure A-6. Coordinate system setup for the B-ring carbon atoms.

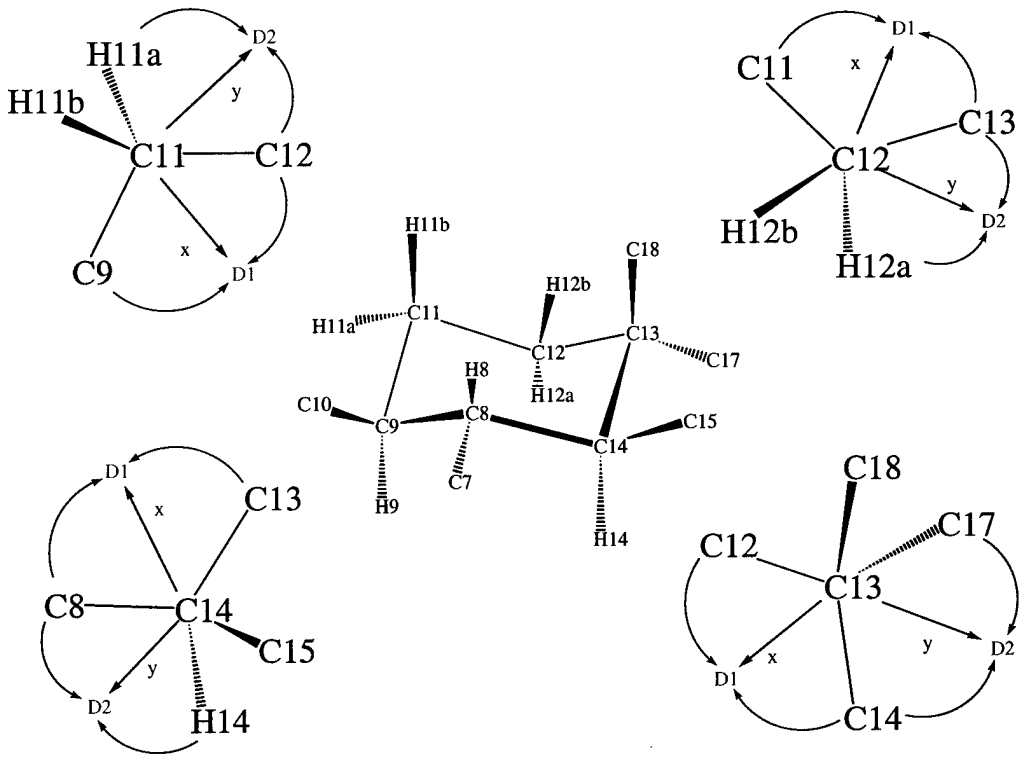

Figure A-7. Coordinate system setup for the C-ring carbon atoms.

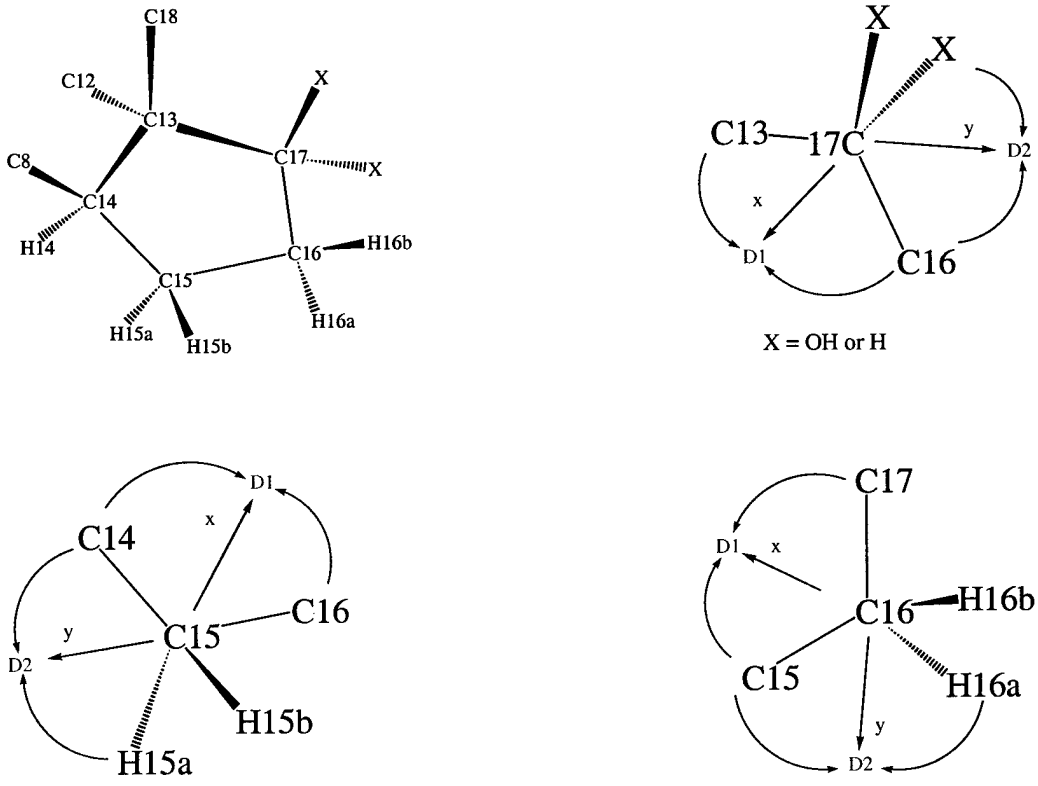

Figure A-8. Coordinate system setup for the D-ring carbon atoms.

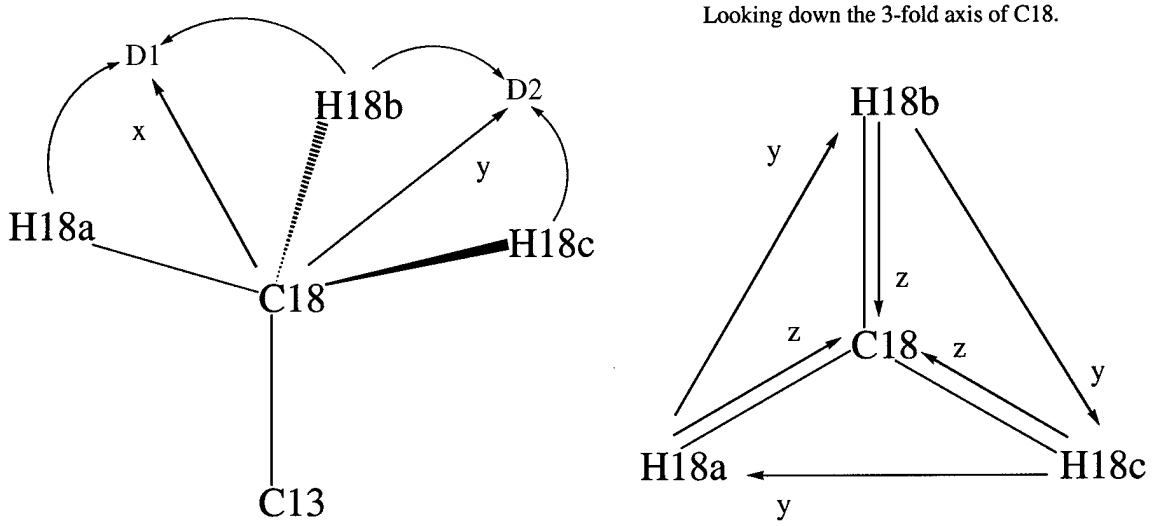

Figure A-9. Coordinate system setup for C18, H18a, H18b, and H18c atoms.

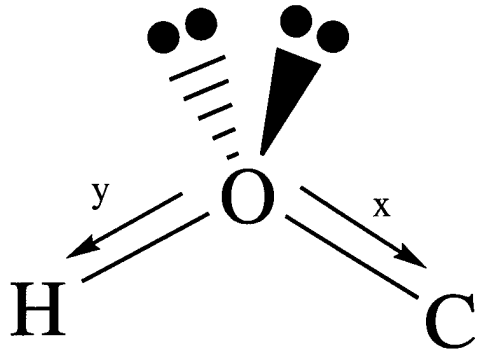

Figure A-10. Coordinate system setup for the hydroxy oxygen atom.

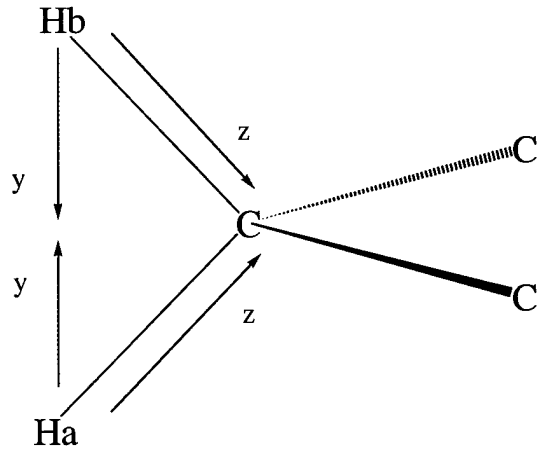

Figure A-11. Coordinate system setup for R_2CH_2 hydrogen atoms. This includes (H6a,H6b),(H7a,H7b),(H11a,H11b),(H12a,H12b),(H15a,H15b), and (H16a,H16b).

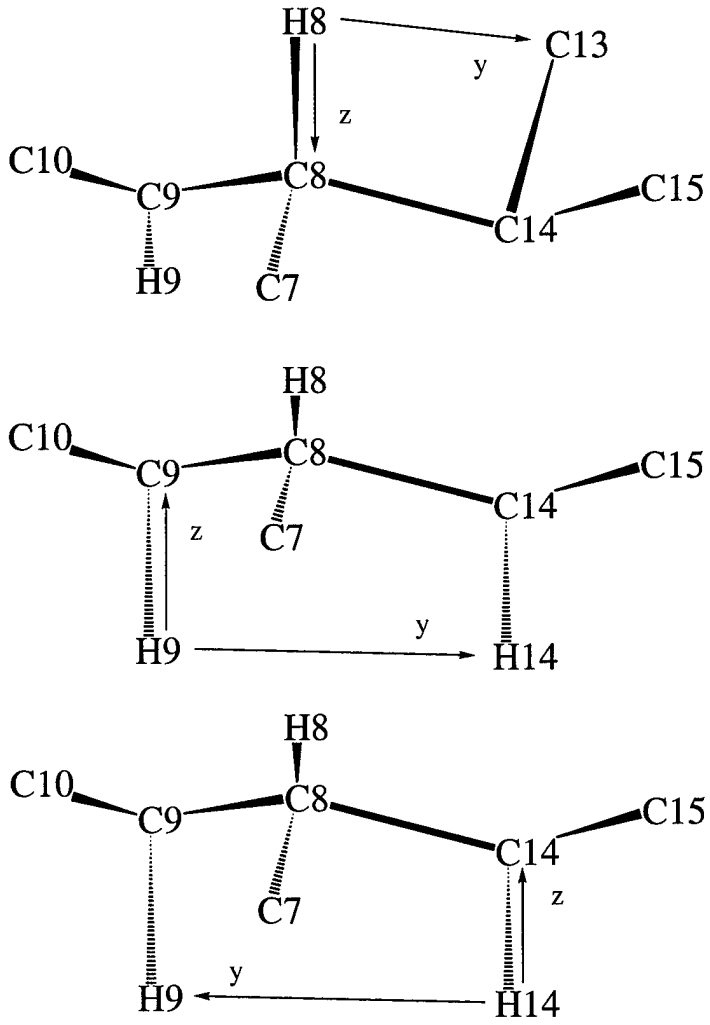

Figure A-12. Coordinate system setup for H8, H9, and H19 atoms.

Appendix B
17β-estradiol•urea

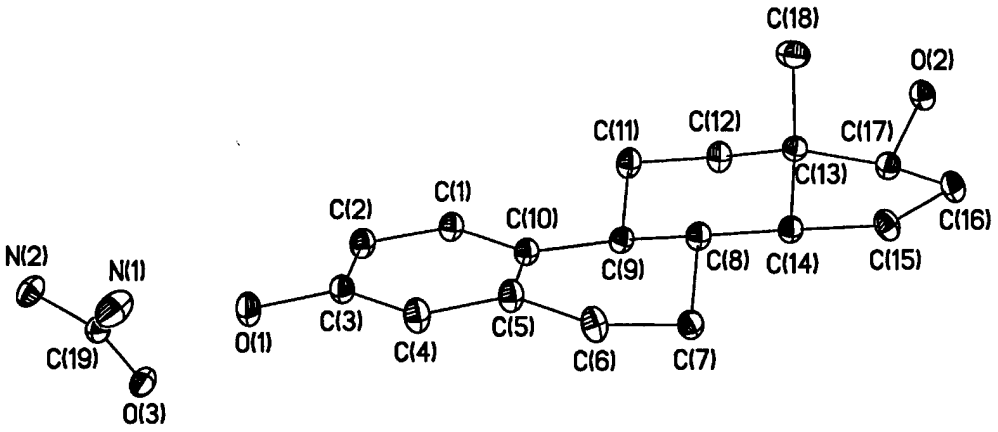

Figure B-1. Thermal ellipsoid plot of 17β-estradiol•urea where ellipsoids represent 50% probability electron density of the atom. Hydrogen atoms are omitted for clarity.

Run	2θ	ω	ϕ	Scan Width (°)	# of Frames	Frame Times (sec)
1	-10	0	45	-0.30	606	60
2	-10	0	135	-0.30	606	60
3	-10	0	225	-0.30	606	60
4	-10	0	315	-0.30	606	60
5	-10	0	45	-0.30	50	60
6	-50	-40	0	-0.30	606	180
7	-50	-40	90	-0.30	606	180
8	-50	-40	180	-0.30	606	180
9	-50	-40	270	-0.30	606	180
10	-50	-40	0	-0.30	50	180
11	-85	-75	22	-0.30	606	180
12	-85	-75	112	-0.30	606	180
13	-85	-75	202	-0.30	606	180
14	-85	-75	292	-0.30	606	180
15	-85	-75	22	-0.30	50	180

Table B-1. Data collection parameters for 17β-estradiol•urea.

Crystal Data			
Chemical Formula	$C_{19}H_{28}N_2O_3$		
Temperature	100.0(1) K		
Crystal Dimensions	0.35 x 0.37 x 0.40 mm		
Space Group	$P2_12_12_1$		
A	7.9022(9) Å		
B	9.2228(10) Å		
C	24.5890(28) Å		
Volume	1792.06(56) $Å^3$		
Z (Crystallographic)	4		
Integration Parameters			
	Box Size (°)	Profile Fitting (I/σ)	Simple Sum Perimeter Limit
Low Angle	1.5 x 1.5 x 1.0	30 10	0.02
Medium Angle	1.2 x 1.2 x 0.8	30 10	0.02
High Angle	1.0 x 1.0 x 0.6	20 10	0.02
Reflection Statistics (from SORTAV)			
Total Reflections	110999		
Rejected Outliers	779		
Unique Reflections	13187		
Average Redundancy	8.4		
Resolution	1.180 $Å^{-1}$		
Completeness	98.6 %		
R_1	3.52 %		
R_2	3.98 %		
R_w	12.84 %		
Z (Refinement)	1.999		

Table B-2. Selected crystal, integration, and reflection data for 17β-estradiol•urea.

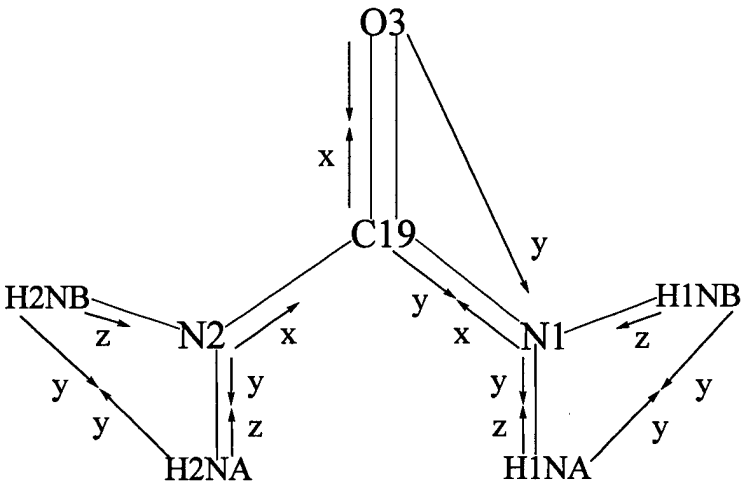

Figure B-2. Coordinate system for the urea molecule.

	n	m	$\langle n \rangle$	R_1	R_2	R_w	Z	V
Q < -4	0	0	0.0	0.0000	0.0000	0.0000	0.000	0.000
-4 < Q < -3	0	0	0.0	0.0000	0.0000	0.0000	0.000	0.000
-3 < Q < -2	0	0	0.0	0.0000	0.0000	0.0000	0.000	0.000
-2 < Q < -1	16	4	4.0	0.5725	0.6015	0.6289	0.924	0.623
-1 < Q < 0	477	118	4.0	1.0875	1.1169	1.0735	1.563	3.758
0 < Q < 1	5750	1091	5.3	0.9343	0.8988	0.8687	1.928	1.597
1 < Q < 2	9331	1649	5.7	0.5575	0.6002	0.5627	1.972	0.654
2 < Q < 3	7669	1278	6.0	0.3519	0.4088	0.3630	2.085	0.391
3 < Q < 4	5953	928	6.4	0.2593	0.3163	0.2643	2.148	0.282
4 < Q < 6	10295	1418	7.3	0.1823	0.2246	0.1892	2.234	0.197
6 < Q < 8	10833	1229	8.8	0.1302	0.1642	0.1397	2.143	0.143
8 < Q < 10	8050	873	9.2	0.1012	0.1272	0.1088	1.990	0.111
10 < Q < 20	22630	2179	10.4	0.0604	0.0737	0.0725	1.867	0.069
20 < Q < 30	13284	1022	13.0	0.0358	0.0498	0.0412	1.337	0.039
30 < Q < 50	15702	984	16.0	0.0236	0.0339	0.0267	1.037	0.027
50 < Q < 100	629	34	18.5	0.0153	0.0216	0.0165	0.975	0.017
100 < Q	0	0	0.0	0.0000	0.0000	0.0000	0.000	0.000

Table B-3. Intensity-Significance Intervals where n is the number of reflections, m is the number of unique reflections, $\langle n \rangle$ is the average measurement multiplicity, and Q=I/Max ($\sigma_{int}/\sigma_{ext}$) respectively for 17$\beta$-estradiol•urea.

	n	m	$\langle n \rangle$	R_1	R_2	R_w	Z	V
D > 1.150	16117	750	21.5	0.0265	0.0399	0.1067	2.013	0.029
1.150 > D > 0.913	9979	699	14.3	0.0259	0.0300	0.1044	1.958	0.031
0.913 > D > 0.798	5817	694	8.4	0.0347	0.0332	0.1071	2.010	0.040
0.798 > D > 0.725	6582	677	9.7	0.0399	0.0382	0.1048	2.012	0.045
0.725 > D > 0.673	8411	672	12.5	0.0482	0.0468	0.1053	2.012	0.055
0.673 > D > 0.633	8720	683	12.8	0.0633	0.0612	0.1137	1.962	0.071
0.633 > D > 0.601	7909	653	12.1	0.0681	0.0590	0.1197	2.020	0.077
0.601 > D > 0.575	7635	663	11.5	0.0872	0.0793	0.1287	2.037	0.097
0.575 > D > 0.553	6763	677	10.0	0.1040	0.0949	0.1445	2.002	0.117
0.553 > D > 0.534	3653	650	5.6	0.1328	0.1375	0.1650	2.042	0.143
0.534 > D > 0.517	3549	642	5.5	0.1489	0.1390	0.1797	2.031	0.167
0.517 > D > 0.502	3458	641	5.4	0.1718	0.1567	0.2036	2.100	0.190
0.502 > D > 0.489	3268	623	5.2	0.2044	0.1875	0.2255	2.066	0.220
0.489 > D > 0.477	3261	650	5.0	0.2160	0.1968	0.2254	2.078	0.232
0.477 > D > 0.466	3002	607	4.9	0.1970	0.1732	0.2134	2.035	0.215
0.466 > D > 0.456	3000	628	4.8	0.2063	0.1610	0.2306	1.955	0.231
0.456 > D > 0.447	2929	614	4.8	0.2780	0.2531	0.2829	1.951	0.307
0.447 > D > 0.439	2646	590	4.5	0.3363	0.3255	0.3274	2.009	0.378
0.439 > D > 0.431	2466	599	4.1	0.3174	0.3091	0.3151	1.957	0.357
0.431 > D > 0.424	1454	395	3.7	0.3788	0.3783	0.3699	2.020	0.435

Table B-4. Equal-Volume Resolution Shells where n is the number of reflections, m is the number of unique reflections, $\langle n \rangle$ is the average measurement multiplicity, and D=sinθ/λ (Å^{-1}) respectively for 17β-estradiol•urea.

	Monopole	sp^2		sp^3
		20	33+	32-
O1	-0.50			
O2	-0.49			
C1	-0.30	-0.22	0.34	
C2	-0.38	-0.19	0.37	
C3	0.27	-0.21	0.38	
C4	-0.33	-0.17	0.36	
C5	-0.18	-0.22	0.33	
C6	-0.26			0.31
C7	-0.31			0.34
C8	-0.21			0.39
C9	-0.17			0.31
C10	-0.25	-0.18	0.37	
C11	-0.31			0.35
C12	-0.28			0.31
C13	-0.16			0.38
C14	-0.20			0.38
C15	-0.26			0.33
C16	-0.35			0.42
C17	0.20			0.38
C18	-0.32			0.27

	Monopole
H1O	0.40
H2O	0.38
H1	0.23
H2	0.22
H4	0.26
H6x	0.20
H7x	0.17
H8	0.20
H9	0.16
H11x	0.17
H12x	0.16
H14	0.19
H15x	0.16
H16x	0.18
H17	0.13
H18x	0.18

Atoms	Kappa	κ	κ'
O1, O2	1	0.97	1.16
C3	2	1.01	0.92
C17	3	1.02	0.95
C1, C2, C4	4	0.97	0.92
C5, C10	5	0.98	0.87
C6, C7, C8, C9, C11, C12, C13, C14, C15, C16, C17, C18	6	0.98	0.95
all C-H hydrogen atoms	7	1.20	1.29
H1O, H2O	8	1.20	1.29
C19	9	0.97	1.00
O3	10	0.98	1.00
N1, N2	11	0.98	1.00
all N-H hydrogen atoms	12	1.02	1.29

Table B-5. Starting values entered into the model for the multipole refinement for 17β-estradiol•urea. Units for multipole populations are e^-.

Atom	X	Y	Z
O1	-0.42058(4)	-0.59511(3)	-0.23303(1)
O2	-0.84199(4)	-0.41994(3)	0.18983(1)
C1	-0.04796(5)	-0.97596(4)	-0.22247(1)
C2	-0.37746(5)	-0.60179(4)	-0.13757(1)
C3	-0.48608(5)	-0.58215(4)	-0.18160(1)
C4	-0.65568(5)	-0.55015(4)	-0.17217(1)
C5	-0.71969(5)	-0.54141(4)	-0.11928(1)
C6	-0.90360(5)	-0.50057(6)	-0.11255(2)
C7	-0.97324(5)	-0.53270(5)	-0.05588(1)
C8	-0.84925(5)	-0.48092(4)	-0.01225(1)
C9	-0.68421(5)	-0.57011(4)	-0.01689(1)
C10	-0.61320(5)	-0.56620(3)	-0.07447(1)
C11	-0.55545(5)	-0.52954(4)	0.02735(1)
C12	-0.63109(5)	-0.53975(4)	0.08481(1)
C13	-0.79262(5)	-0.44893(3)	0.08951(1)
C14	-0.91843(5)	-0.49685(4)	0.04520(1)
C15	-1.08387(5)	-0.41986(5)	0.06157(2)
C16	-1.07772(5)	-0.41828(5)	0.12477(2)
C17	-0.90256(5)	-0.48028(4)	0.13965(1)
C18	-0.75013(6)	-0.28663(4)	0.08704(2)
O3	-0.04796(4)	-0.97596(3)	-0.22247(1)
N1	-0.09659(6)	-0.74930(4)	-0.25468(2)
N2	0.16786(5)	-0.85170(4)	-0.26106(2)
C19	0.00538(5)	-0.86273(4)	-0.24498(1)

Atom	X	Y	Z
H1O	-0.5100(10)	-0.5903(7)	-0.2600(3)
H2O	-0.7423(10)	-0.4751(7)	0.2000(3)
H1	-0.3549(9)	-0.6105(6)	-0.0517(2)
H2	-0.2452(9)	-0.6251(7)	-0.1443(3)
H4	-0.7400(8)	-0.5358(6)	-0.2063(2)
H6A	-0.9774(9)	-0.5601(7)	-0.1426(3)
H6B	-0.9100(9)	-0.3835(7)	-0.1182(3)
H7A	-0.9929(9)	-0.6490(6)	-0.0510(2)
H7B	-1.0948(9)	-0.4788(6)	-0.0504(2)
H8	-0.8208(8)	-0.3662(7)	-0.0205(2)
H9	-0.7189(8)	-0.6835(6)	-0.0087(2)
H11A	-0.4469(9)	-0.6024(7)	0.0259(2)
H11B	-0.5063(8)	-0.4209(6)	0.0200(2)
H12A	-0.6637(9)	-0.6524(6)	0.0932(2)
H12B	-0.5379(8)	-0.5075(6)	0.1152(2)
H14	-0.9378(9)	-0.6138(6)	0.0513(2)
H15A	-1.1956(9)	-0.4791(7)	0.0481(3)
H15B	-1.0837(9)	-0.3087(6)	0.0465(2)
H16A	-1.1756(9)	-0.4867(7)	0.1426(3)
H16B	-1.0881(9)	-0.3060(7)	0.1382(2)
H17	-0.9091(7)	-0.5985(6)	0.1453(2)
H18A	-0.6610(9)	-0.2590(7)	0.1175(3)
H18B	-0.8580(9)	-0.2196(7)	0.0920(3)
H18C	-0.6952(9)	-0.2570(6)	0.0493(2)
H1NA	-0.0501(9)	-0.6536(8)	-0.2679(3)
H1NB	-0.2166(11)	-0.7532(7)	-0.2406(3)
H2NA	0.2092(9)	-0.7646(7)	-0.2821(3)
H2NB	0.2465(9)	-0.9373(7)	-0.2569(2)

Table B-6. Fractional atomic coordinates for 17β-estradiol•urea.

Atom	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.01219(10)	0.02443(12)	0.01244(9)	0.00174(11)	0.00131(8)	-0.00125(8)
O2	0.01461(11)	0.02036(11)	0.01108(9)	0.00249(10)	-0.00183(8)	-0.00162(8)
C1	0.00957(12)	0.01862(13)	0.01219(12)	0.00164(11)	-0.00066(10)	0.00125(10)
C2	0.00983(13)	0.02011(14)	0.01349(12)	0.00185(12)	0.00006(10)	0.00039(10)
C3	0.01021(13)	0.01712(13)	0.01145(11)	0.00099(12)	0.00042(10)	-0.00055(9)
C4	0.01090(13)	0.02641(16)	0.01081(12)	0.00325(13)	-0.00012(10)	-0.00051(10)
C5	0.00961(13)	0.02420(15)	0.01106(12)	0.00309(12)	-0.00084(10)	-0.00021(10)
C6	0.01117(14)	0.04863(26)	0.01159(13)	0.00858(18)	-0.00129(11)	0.00116(14)
C7	0.00921(13)	0.02872(17)	0.01277(12)	0.00087(14)	-0.00135(10)	-0.00267(11)
C8	0.00961(12)	0.01643(12)	0.01109(11)	0.00090(11)	-0.00096(10)	0.00023(9)
C9	0.00978(12)	0.01527(12)	0.01158(11)	0.00015(11)	-0.00077(9)	0.00087(9)
C10	0.00897(12)	0.01541(12)	0.01155(11)	0.00117(11)	-0.00080(9)	0.00038(9)
C11	0.00970(13)	0.02408(16)	0.01227(12)	0.00005(13)	-0.00152(10)	0.00010(11)
C12	0.01189(13)	0.02230(15)	0.01171(12)	0.00316(13)	-0.00168(10)	0.00088(10)
C13	0.01115(13)	0.01363(12)	0.01124(11)	-0.00017(11)	-0.00106(10)	-0.00017(9)
C14	0.01021(13)	0.01698(13)	0.01142(11)	-0.00030(11)	-0.00072(10)	-0.00060(9)
C15	0.01228(15)	0.03705(21)	0.01294(13)	0.00648(16)	-0.00145(11)	-0.00237(13)
C16	0.01284(15)	0.03791(21)	0.01290(13)	0.00506(16)	-0.00006(12)	-0.00300(13)
C17	0.01249(14)	0.01785(13)	0.01145(11)	0.00011(13)	-0.00036(10)	-0.00014(10)
C18	0.02583(21)	0.01531(13)	0.01719(15)	-0.00386(14)	-0.00059(14)	-0.00085(11)
O3	0.01596(12)	0.01799(11)	0.02292(12)	-0.00185(11)	0.00584(10)	0.00228(9)
N1	0.01700(17)	0.01705(14)	0.04896(23)	0.00427(14)	0.00785(17)	0.00300(14)
N2	0.01356(14)	0.01725(13)	0.02797(15)	0.00033(12)	0.00619(12)	0.00426(11)
C19	0.01344(15)	0.01475(12)	0.01804(13)	-0.00048(12)	0.00345(12)	-0.00102(10)

Table B-7. Anisotropic thermal parameters of non-H atoms for 17β-estradiol•urea.

Atom	U_{iso}
H1O	0.0232(16)
H2O	0.0252(17)
H1	0.0499(16)
H2	0.0456(16)
H4	0.0406(15)
H6A	0.0711(19)
H6B	0.0651(18)
H7A	0.0524(16)
H7B	0.0506(15)
H8	0.0465(15)
H9	0.0482(16)
H11A	0.0613(17)
H11B	0.0479(14)
H12A	0.0544(16)
H12B	0.0524(15)

Atom	U_{iso}
H14	0.0401(14)
H15A	0.0637(18)
H15B	0.0531(16)
H16A	0.0675(19)
H16B	0.0570(17)
H17	0.0501(14)
H18A	0.0631(18)
H18B	0.0629(17)
H18C	0.0596(17)
H1NA	0.0471(18)
H1NB	0.0509(19)
H2NA	0.0437(17)
H2NB	0.0448(17)

Table B-8. Isotropic thermal parameters of H atoms for 17β-estradiol•urea.

Atoms	Bond Length (Å)
O1 – C3	1.3716(4)
O2 – C17	1.4357(4)
C1 – C2	1.3923(5)
C1 – C10	1.4013(5)
C2 – C3	1.3934(5)
C3 – C4	1.3918(5)
C4 – C5	1.3977(5)
C5 – C6	1.5104(6)
C5 – C10	1.4051(5)
C6 – C7	1.5272(5)
C7 – C8	1.5294(5)
C8 – C9	1.5461(5)
C8 – C14	1.5219(5)

Atoms	Bond Length (Å)
C9 – C10	1.5235(5)
C9 – C11	1.5357(5)
C11 – C12	1.5368(5)
C12 – C13	1.5312(5)
C13 – C14	1.5398(5)
C13 – C17	1.5357(5)
C13 – C18	1.5352(5)
C14 – C15	1.5412(6)
C15 – C16	1.5550(5)
C16 – C17	1.5417(6)
O3 – C19	1.2547(5)
N1 – C19	1.3419(6)
N2 – C19	1.3474(5)

Table B-9. Bond distances of non-H atoms of 17β-estradiol•urea.

Atoms	Bond Angle (°)
C3 – O1 – H1O	110.6(5)
C17 – O2 – H2O	106.7(5)
C2 – C1 – C10	122.3(1)
C2 – C1 – H1	117.6(4)
C10 – C1 – H1	120.1(4)
C1 – C2 – C3	119.3(1)
C1 – C2 – H2	120.5(4)
C3 – C2 – H2	120.2(4)
O1 – C3 – C2	118.2(1)
O1 – C3 – C4	122.4(1)
C2 – C3 – C4	119.4(1)
C3 – C4 – C5	121.0(1)
C3 – C4 – H4	119.4(4)
C5 – C4 – H4	119.5(4)
C4 – C5 – C6	117.7(1)
C4 – C5 – C10	120.2(1)
C6 – C5 – C10	122.1(1)
C5 – C6 - C7	113.5(1)
C5 – C6 – H6A	108.3(4)
C5 – C6 – H6B	106.1(4)
C7 – C6 – H6A	109.2(4)
C7 – C6 – H6B	106.9(4)
H6A – C6 – H6B	112.8(6)
C6 – C7 – C8	110.4(1)
C6 – C7 – H7A	110.0(4)
C6 – C7 – H7B	110.0(3)
C8 – C7 – H7A	108.8(4)
C8 – C7 – H7B	109.6(4)
H7A – C7 – H7B	108.0(5)
C7 – C8 – C9	108.8(1)
C7 – C8 – C14	113.0(1)
C9 – C8 – C14	108.7(1)
C7 – C8 – H8	107.6(4)
C9 – C8 – H8	109.0(4)

Atoms	Bond Angle (°)
C14 – C8 – H8	109.7(3)
C8 – C9 – C10	111.5(1)
C8 – C9 – C11	112.2(1)
C10 – C9 – C11	114.1(1)
C8 – C9 – H9	106.4(4)
C10 – C9 – H9	106.6(4)
C11 – C9 – H9	105.4(4)
C1 – C10 – C5	117.6(1)
C1 – C10 – C9	121.5(1)
C5 – C10 – C9	120.8(1)
C9 – C11 – C12	112.2(1)
C9 – C11 – H11A	110.4(4)
C9 – C11 – H11B	110.0(3)
C12 – C11 – H11A	107.3(4)
C12 – C11 – H11B	110.4(3)
H11A – C11 – H11B	106.3(5)
C11 – C12 – C13	111.1(1)
C11 – C12 – H12A	109.0(4)
C11 – C12 – H12B	110.5(4)
C13 – C12 – H12A	108.0(4)
C13 – C12 – H12B	111.2(4)
H12A – C12 – H12B	106.8(5)
C12 – C13 – C14	109.1(1)
C12 – C13 – C17	115.4(1)
C12 – C13 – C18	110.4(1)
C14 – C13 – C17	98.6(1)
C14 – C13 – C18	113.1(1)
C17 – C13 – C18	109.8(1)
C8 – C14 – C13	113.4(1)
C8 – C14 – C15	120.2(1)
C13 – C14 – C15	103.3(1)
C8 – C14 – H14	105.8(3)
C13 – C14 – H14	105.9(4)
C15 – C14 – H14	107.3(4)

Atoms	Bond Angle (°)
C14 – C15 – C16	103.8(1)
C14 – C15 – H15A	112.1(4)
C14 – C15 – H15B	110.1(4)
C16 – C15 – H15A	109.5(4)
C16 – C15 – H15B	109.3(4)
H15A – C15 – H15B	111.7(6)
C15 – C16 – C17	105.2(1)
C15 – C16 – H16A	111.9(4)
C15 – C16 – H16B	108.1(4)
C17 – C16 – H16A	109.1(4)
C17 – C16 – H16B	110.4(4)
H16A – C16 – H16B	112.0(6)
O2 – C17 – C13	115.4(1)
O2 – C17 – C16	111.1(1)
C13 – C17 – C16	104.3(1)
O2 – C17 – H17	106.9(3)
C13 – C17 – H17	108.3(3)
C16 – C17 – H17	110.8(4)
C13 – C18 – H18A	110.6(4)
C13 – C18 – H18B	112.8(4)
C13 – C18 – H18C	112.1(4)
H18A – C18 – H18B	108.2(6)
H18A – C18 – H18C	106.6(6)
H18B – C18 – H18C	106.2(6)
O3 – C19 – N1	121.7(1)
O3 – C19 – N2	120.8(1)
N1 – C19 – N2	121.4(1)
C19 – N1 – H1NA	118.4(5)
C19 – N1 – H1NB	118.9(5)
H1NA – N1 – H1NB	121.2(6)
C19 – N2 – H2NA	121.4(5)
C19 – N2 – H2NB	119.8(5)
H2NA – N2 – H2NB	118.4(6)

Table B-10. Bond angles of 17β-estradiol•urea.

Atom	Monopole Population ($P_{0,0}$)
O1	6.534(9)
O2	6.527(9)
C1	4.233(16)
C2	4.227(16)
C3	3.852(14)
C4	4.267(15)
C5	4.110(15)
C6	4.265(16)
C7	4.279(16)
C8	4.121(14)
C9	4.131(15)
C10	4.106(15)
C11	4.277(15)
C12	4.273(15)
C13	4.158(16)
C14	4.111(14)
C15	4.294(15)
C16	4.273(16)
C17	3.832(13)
C18	4.402(17)
O3	6.234(9)
N1	5.282(12)
N2	5.286(11)
C19	4.030(14)

Atom	Monopole Population ($P_{0,0}$)
H1O	0.599(9)
H2O	0.609(9)
H1	0.794(10)
H2	0.752(9)
H4	0.751(9)
H6A	0.853(7)
H6B	0.853(7)
H7A	0.854(7)
H7B	0.854(7)
H8	0.820(9)
H9	0.820(9)
H11A	0.853(7)
H11B	0.853(7)
H12A	0.859(7)
H12B	0.859(7)
H14	0.824(8)
H15A	0.851(7)
H15B	0.851(7)
H16A	0.854(7)
H16B	0.854(7)
H17	0.880(9)
H18A	0.878(6)
H18B	0.878(6)
H18C	0.878(6)
H1NA	0.795(10)
H1NB	0.791(11)
H2NA	0.793(10)
H2NB	0.792(10)

Table B-11. Monopole populations (e^-) of 17β-estradiol•urea.

Multipoles	O1	O2	O3	N1	N2
$P_{1,+1}$	-0.017(8)	-0.069(7)	-0.095(6)	0.037(10)	0.0
$P_{1,-1}$	0.0	-0.029(7)	-0.021(6)	0.0	-0.011(10)
$P_{1,0}$	0.0	0.023(7)	-0.016(5)	0.051(8)	-0.040(7)
$P_{2,0}$	0.089(8)	0.078(8)	-0.089(7)	-0.048(9)	-0.032(8)
$P_{2,+1}$	-0.013(8)	0.026(8)	0.0	-0.051(10)	0.018(9)
$P_{2,-1}$	-0.023(9)	0.035(7)	0.043(7)	0.0	0.0
$P_{2,+2}$	-0.036(8)	-0.047(8)	-0.073(7)	0.045(10)	0.0
$P_{2,-2}$	0.0	0.015(8)	-0.018(8)	0.0	0.0
$P_{3,0}$	0.0	0.056(14)	0.031(11)	0.049(13)	-0.043(12)
$P_{3,+1}$	-0.037(10)	0.0	0.017(10)	0.061(12)	-0.060(12)
$P_{3,-1}$	-0.051(10)	-0.052(10)	-0.041(10)	0.0	0.0
$P_{3,+2}$	0.027(14)	-0.011(10)	0.0	-0.084(15)	0.0
$P_{3,-2}$	0.031(14)	0.0	0.0	-0.024(13)	0.024(12)
$P_{3,+3}$	0.101(10)	0.069(12)	0.0	0.155(11)	0.167(10)
$P_{3,-3}$	-0.059(11)	-0.028(10)	0.018(10)	0.0	0.0
$P_{4,0}$	0.041(13)	-0.031(14)			
$P_{4,+1}$	-0.036(13)	0.022(13)			
$P_{4,-1}$	0.0	0.016(13)			
$P_{4,+2}$	-0.025(13)	0.038(12)			
$P_{4,-2}$	0.0	-0.017(12)			
$P_{4,+3}$	0.029(14)	-0.025(13)			
$P_{4,-3}$	0.0	0.0			
$P_{4,+4}$	0.020(12)	0.020(12)			
$P_{4,-4}$	-0.020(12)	-0.042(13)			

Table B-12. Multipole populations (e^-) of Oxygen and Nitrogen atoms of 17β-estradiol•urea.

Multipoles	C1	C2	C3	C4	C5	C6	C7	C8	C9
$P_{1,+1}$	0.069(15)	0.073(14)	0.037(16)	0.0	0.052(16)	-0.074(13)	-0.057(13)	0.013(12)	0.035(12)
$P_{1,-1}$	0.0	-0.038(15)	0.067(14)	0.046(16)	0.052(16)	0.0	0.0	0.0	0.0
$P_{1,0}$	0.0	0.019(13)	0.0	-0.041(13)	-0.058(14)	-0.092(13)	-0.047(12)	0.013(12)	0.069(13)
$P_{2,0}$	-0.228(11)	-0.189(11)	-0.191(11)	-0.192(11)	-0.231(12)	-0.042(15)	-0.012(12)	0.0	0.056(13)
$P_{2,+1}$	0.0	0.0	0.0	0.023(13)	-0.038(14)	-0.037(12)	-0.019(11)	0.0	0.023(12)
$P_{2,-1}$	0.048(13)	0.021(13)	0.036(12)	0.0	0.0	0.059(12)	0.0	0.0	0.0
$P_{2,+2}$	0.057(14)	0.0	0.054(14)	0.062(14)	0.047(15)	0.105(12)	0.071(11)	0.023(11)	0.023(12)
$P_{2,-2}$	0.0	0.067(14)	-0.059(14)	-0.056(14)	0.023(15)	0.022(13)	0.0	-0.015(12)	0.0
$P_{3,0}$	-0.034(16)	-0.022(16)	0.0	0.0	-0.029(18)	-0.064(17)	0.034(17)	0.050(18)	0.048(17)
$P_{3,+1}$	-0.042(15)	0.0	0.0	0.0	0.043(17)	0.022(18)	-0.166(15)	0.0	0.046(17)
$P_{3,-1}$	0.021(15)	0.0	0.022(15)	0.0	0.023(17)	0.0	0.015(14)	0.0	0.177(15)
$P_{3,+2}$	-0.024(20)	0.018(20)	0.0	0.0	0.056(23)	0.035(16)	0.0	0.0	-0.116(16)
$P_{3,-2}$	-0.025(20)	0.034(17)	-0.074(22)	0.036(19)	0.0	0.310(15)	0.254(15)	0.388(15)	0.320(15)
$P_{3,+3}$	0.365(15)	0.328(15)	0.351(15)	0.342(15)	0.313(15)	-0.208(15)	-0.189(16)	0.027(15)	0.120(15)
$P_{3,-3}$	-0.036(19)	0.0	0.075(22)	0.050(19)	0.0	-0.029(17)	0.0	-0.031(17)	0.0

Multipoles	C10	C11	C12	C13	C14	C15	C16	C17	C18	C19
$P_{1,+1}$	0.068(18)	-0.079(13)	-0.017(12)	0.0	-0.045(14)	-0.052(14)	-0.051(14)	-0.019(11)	0.066(11)	0.145(14)
$P_{1,-1}$	-0.028(15)	-0.050(11)	-0.034(13)	0.059(13)	0.035(12)	0.077(12)	-0.023(13)	0.042(12)	0.024(12)	-0.023(16)
$P_{1,0}$	-0.026(13)	0.011(11)	0.0	-0.030(12)	-0.084(13)	-0.079(12)	-0.096(12)	-0.071(12)	0.0	-0.059(13)
$P_{2,0}$	-0.230(11)	0.0	0.0	-0.020(12)	-0.014(12)	-0.038(13)	-0.092(11)	0.0	-0.052(12)	-0.377(12)
$P_{2,+1}$	-0.020(15)	-0.053(12)	0.038(11)	-0.026(12)	0.035(12)	0.033(11)	0.0	0.069(11)	0.043(12)	0.0
$P_{2,-1}$	0.021(13)	0.019(11)	0.033(13)	0.0	0.0	0.023(12)	0.020(13)	0.0	0.0	-0.022(13)
$P_{2,+2}$	0.060(15)	0.063(11)	0.039(12)	0.0	0.034(11)	0.083(12)	0.068(12)	0.020(11)	0.022(10)	0.166(15)
$P_{2,-2}$	-0.036(15)	-0.032(11)	0.052(12)	0.0	-0.043(13)	-0.020(12)	-0.016(11)	0.0	-0.011(11)	0.0
$P_{3,0}$	0.060(16)	0.026(15)	0.018(14)	0.0	-0.023(17)	0.054(19)	-0.045(16)	-0.041(15)	-0.023(15)	0.0
$P_{3,+1}$	-0.031(17)	-0.111(16)	-0.105(14)	0.0	-0.049(16)	0.0	0.0	-0.110(14)	0.0	-0.082(16)
$P_{3,-1}$	0.036(15)	-0.027(14)	-0.037(17)	0.0	0.061(16)	0.055(16)	0.064(17)	0.028(16)	0.0	-0.074(18)
$P_{3,+2}$	-0.023(20)	-0.058(16)	0.040(16)	0.066(17)	0.026(16)	0.0	-0.029(18)	0.073(15)	0.023(18)	-0.020(19)
$P_{3,-2}$	-0.082(24)	0.351(16)	0.375(15)	0.472(15)	0.334(14)	0.330(15)	0.337(15)	0.329(14)	0.265(14)	0.025(19)
$P_{3,+3}$	0.358(16)	-0.173(14)	-0.100(16)	0.035(17)	-0.105(17)	-0.170(16)	-0.130(16)	-0.022(16)	0.049(13)	0.500(18)
$P_{3,-3}$	0.038(24)	0.0	0.0	-0.025(18)	-0.056(16)	0.0	0.017(16)	-0.042(15)	-0.050(13)	0.0

Table B-13. Multipole populations (e^-) of Carbon atoms of 17β-estradiol•urea.

Atoms	$P_{1,0}$	$P_{2,0}$
H1O	0.130(11)	0.023(14)
H2O	0.121(11)	0.026(14)
H1	0.152(13)	0.0
H2	0.117(13)	0.026(15)
H4	0.172(12)	0.0
H6A	0.131(9)	0.052(10)
H6B	0.131(9)	0.052(10)
H7A	0.117(9)	0.036(10)
H7B	0.117(9)	0.036(10)
H8	0.148(11)	0.113(15)
H9	0.106(12)	0.023(15)
H11A	0.122(8)	0.040(11)
H11B	0.122(8)	0.040(11)
H12A	0.138(8)	0.0
H12B	0.138(8)	0.0
H14	0.076(11)	0.047(13)
H15A	0.105(8)	0.035(11)
H15B	0.105(8)	0.035(11)
H16A	0.131(8)	0.044(11)
H16B	0.131(8)	0.044(11)
H17	0.183(11)	0.076(15)
H18A	0.126(6)	-0.032(9)
H18B	0.126(6)	-0.032(9)
H18C	0.126(6)	-0.032(9)
H1NA	0.152(14)	0.077(17)
H1NB	0.164(15)	0.025(18)
H2NA	0.162(13)	0.0
H2NB	0.189(13)	0.097(19)

Table B-14. Multipole populations (e^-) of Hydrogen atoms of 17β-estradiol•urea.

Bond	$\rho(r_c)$	$\nabla^2\rho(r_c)$	R_{ij}	d_1	d_2	λ_1	λ_2	λ_3	ε
O1 – C3	2.087	-18.278	1.3735	0.8406	0.5328	-16.40	-15.05	13.17	0.09
O1 – H1O	2.283	-34.847	0.9701	0.7549	0.2152	-37.51	-37.10	39.76	0.01
O2 – C17	1.739	-7.066	1.4361	0.8207	0.6155	-12.61	-11.76	17.30	0.07
O2 – H2O	2.221	-30.002	0.9702	0.7490	0.2212	-35.29	-35.22	40.50	0.00
C1 – C2	2.188	-21.224	1.3923	0.7537	0.6387	-16.15	-13.34	8.26	0.21
C1 – C10	2.184	-20.509	1.4015	0.6771	0.7244	-16.21	-13.19	8.89	0.23
C1 – H1	1.945	-17.399	1.0805	0.6484	0.4321	-17.84	-16.23	16.67	0.10
C2 – C3	2.201	-20.558	1.3942	0.6970	0.6972	-16.73	-13.50	9.67	0.24
C2 – H2	1.947	-17.412	1.0801	0.6725	0.4076	-18.63	-16.82	18.03	0.11
C3 – C4	2.238	-21.298	1.3919	0.6954	0.6965	-17.37	-13.58	9.66	0.28
C4 – C5	2.144	-19.321	1.3977	0.7275	0.6702	-15.37	-12.94	8.99	0.19
C4 – H4	1.890	-17.235	1.0801	0.6420	0.4381	-17.00	-15.60	15.37	0.09
C5 – C6	1.753	-12.498	1.5104	0.7542	0.7562	-11.87	-10.85	10.22	0.09
C5 – C10	2.073	-17.563	1.4056	0.7242	0.6815	-15.00	-11.83	9.27	0.27
C6 – C7	1.671	-10.333	1.5286	0.7841	0.7445	-10.68	-10.23	10.57	0.04
C6 – H6A	1.831	-12.619	1.0908	0.6435	0.4473	-16.09	-13.33	16.81	0.11
C6 – H6B	1.831	-12.619	1.0908	0.6435	0.4473	-16.09	-13.33	16.81	0.11
C7 – C8	1.655	-9.901	1.5299	0.7729	0.7570	-10.35	-10.04	10.48	0.03
C7 – H7A	1.899	-15.061	1.0906	0.6524	0.4382	-16.77	-15.49	17.19	0.08
C7 – H7B	1.857	-14.569	1.0914	0.6503	0.4411	-16.31	-15.35	17.09	0.06
C8 – C9	1.642	-10.327	1.5466	0.7799	0.7667	-10.36	-10.25	10.28	0.01
C8 – C14	1.653	-10.798	1.5222	0.7755	0.7467	-10.81	-10.02	10.03	0.08
C8 – H8	1.937	-19.600	1.1001	0.6447	0.4554	-17.43	-16.44	14.27	0.06
C9 – C10	1.667	-10.503	1.5240	0.7527	0.7714	-10.93	-9.81	10.24	0.11
C9 – C11	1.701	-11.816	1.5360	0.7469	0.7891	-11.33	-10.80	10.31	0.05
C9 – H9	1.900	-15.526	1.1001	0.6725	0.4276	-17.18	-15.99	17.64	0.07

Table B-15. Topological properties of bond critical points in 17β-estradiol•urea.

Bond	$\rho(r_c)$	$\nabla^2\rho(r_c)$	R_{ij}	d_1	d_2	λ_1	λ_2	λ_3	ε
C11 – C12	1.625	-10.611	1.5370	0.7554	0.7816	-10.64	-10.04	10.06	0.06
C11 – H11A	1.881	-15.797	1.0915	0.6470	0.4445	-16.59	-15.64	16.44	0.06
C11 – H11B	1.965	-16.576	1.0900	0.6560	0.4340	-17.75	-16.24	17.42	0.09
C12 – C13	1.752	-12.334	1.5312	0.7736	0.7576	-11.75	-10.99	10.41	0.07
C12 – H12A	1.857	-14.791	1.0903	0.6392	0.4511	-15.65	-15.34	16.19	0.02
C12 – H12B	1.906	-15.838	1.0900	0.6430	0.4471	-16.66	-15.56	16.38	0.07
C13 – C14	1.678	-10.846	1.5405	0.7759	0.7647	-10.60	-10.46	10.21	0.01
C13 – C17	1.663	-10.699	1.5358	0.7920	0.7438	-11.24	-10.15	10.69	0.11
C13 – C18	1.643	-10.505	1.5353	0.7848	0.7505	-10.43	-10.33	10.26	0.01
C14 – C15	1.576	-8.910	1.5423	0.7492	0.7931	-10.33	-8.94	10.37	0.16
C14 – H14	1.833	-13.737	1.1001	0.6774	0.4227	-16.23	-15.71	18.21	0.03
C15 – C16	1.629	-10.671	1.5555	0.7848	0.7707	-10.72	-10.25	10.30	0.05
C15 – H15A	1.927	-14.910	1.0912	0.6642	0.4270	-17.76	-15.56	18.41	0.14
C15 – H15B	1.680	-10.886	1.0926	0.6398	0.4528	-14.44	-12.82	16.37	0.13
C16 – C17	1.636	-9.386	1.5418	0.7812	0.7606	-10.89	-9.84	11.34	0.11
C16 – H16A	1.917	-15.675	1.0909	0.6486	0.4422	-17.37	-15.14	16.84	0.15
C16 – H16B	1.774	-13.036	1.0948	0.6419	0.4529	-15.39	-14.15	16.50	0.09
C17 – H17	2.064	-20.314	1.1003	0.6508	0.4495	-19.34	-18.25	17.28	0.06
C18 – H18A	1.862	-12.496	1.0608	0.6180	0.4428	-15.33	-14.17	17.01	0.08
C18 – H18B	1.922	-13.177	1.0602	0.6249	0.4353	-16.19	-14.80	17.81	0.09
C18 – H18C	1.878	-13.292	1.0602	0.6181	0.4421	-15.73	-14.50	16.94	0.08
O3 – C19	2.767	-31.828	1.2548	0.8156	0.4392	-24.24	-23.53	15.94	0.03
N1 – C19	2.261	-24.734	1.3424	0.8749	0.4675	-17.80	-16.90	9.97	0.05
N2 – C19	2.266	-24.089	1.3476	0.8745	0.4731	-18.03	-15.38	9.32	0.17
N1 – H1NA	2.407	-28.058	1.0101	0.7172	0.2929	-31.73	-30.39	34.06	0.04
N1 – H1NB	2.370	-23.814	1.0100	0.7135	0.2965	-30.34	-28.21	34.74	0.08
N2 – H2NA	2.333	-21.488	1.0100	0.7113	0.2987	-29.51	-27.12	35.14	0.09
N2 – H2NB	2.494	-31.772	1.0100	0.7153	0.2947	-33.39	-31.38	33.00	0.06

Table B-16. Topological properties of bond critical points in 17β-estradiol•urea continued.

Bond	$\rho(r_c)$	$\nabla^2\rho(r_c)$	R_{ij}	d_1	d_2	λ_1	λ_2	λ_3	ε
O2—**H2O··O3**	0.230	4.624	1.6951	0.5589	1.1362	-1.47	-1.42	7.52	0.04
O1—**H1O··O2**	0.208	4.795	1.7027	0.5510	1.1516	-1.27	-1.18	7.24	0.08
N1—**H1NA··O3**	0.210	2.909	1.8274	0.6530	1.1744	-1.34	-1.31	5.57	0.02
N1—**H1NB··O1**	0.085	1.751	2.2050	0.8369	1.3681	-0.42	-0.34	2.51	0.24
N2—**H2NB··O1**	0.129	1.702	2.0179	0.7221	1.2957	-0.79	-0.73	3.23	0.08
N2—**H2NA··O2**	0.064	2.101	2.1200	0.7459	1.3740	-0.31	-0.24	2.66	0.29

Table B-17. Topological properties of bond critical points in the hydrogen bonds of 17β-estradiol•urea.

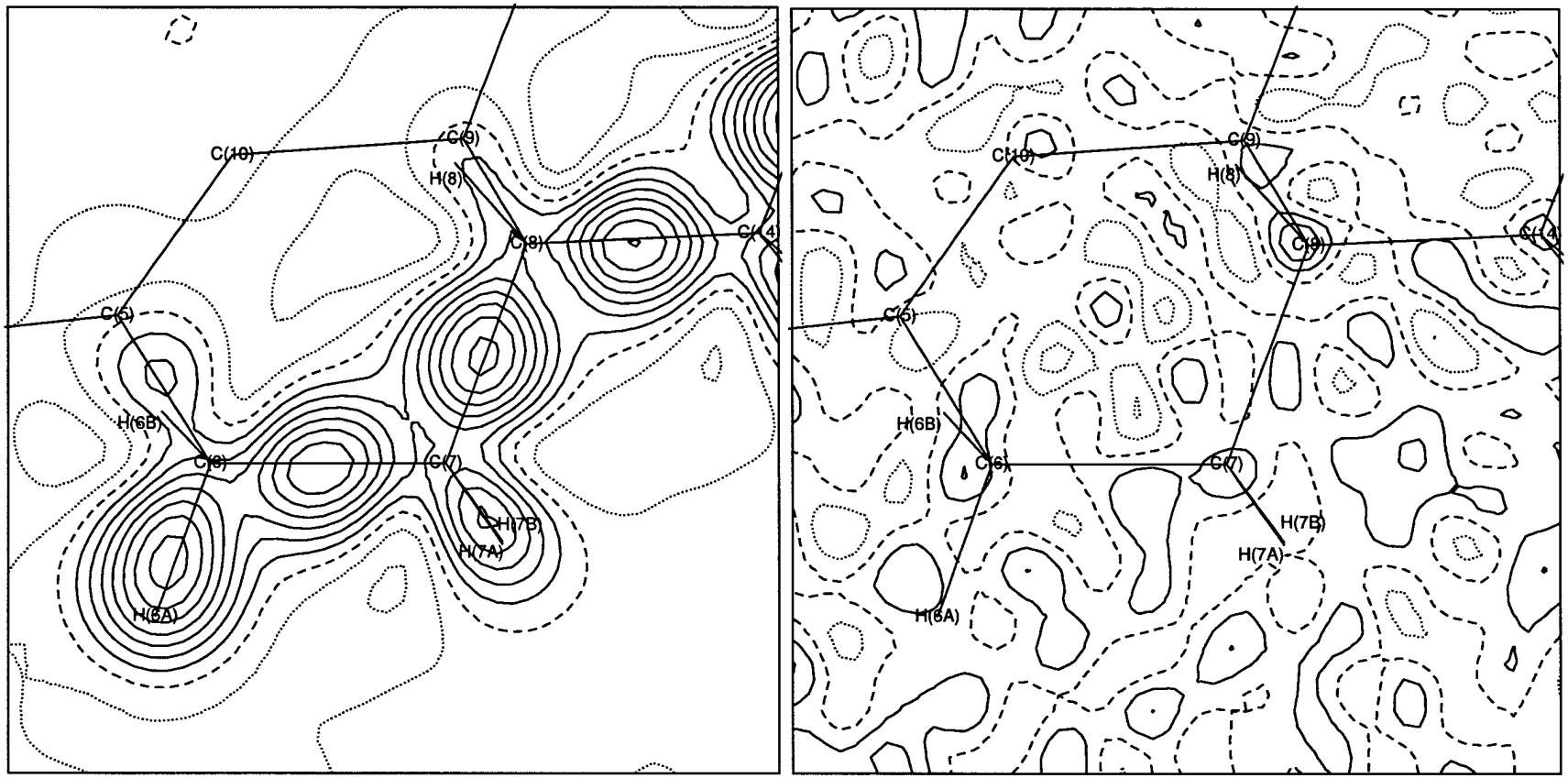

Figure B-3. Dynamic model map and residual map in the C6 – C7 – C8 plane of 17β-estradiol•urea. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

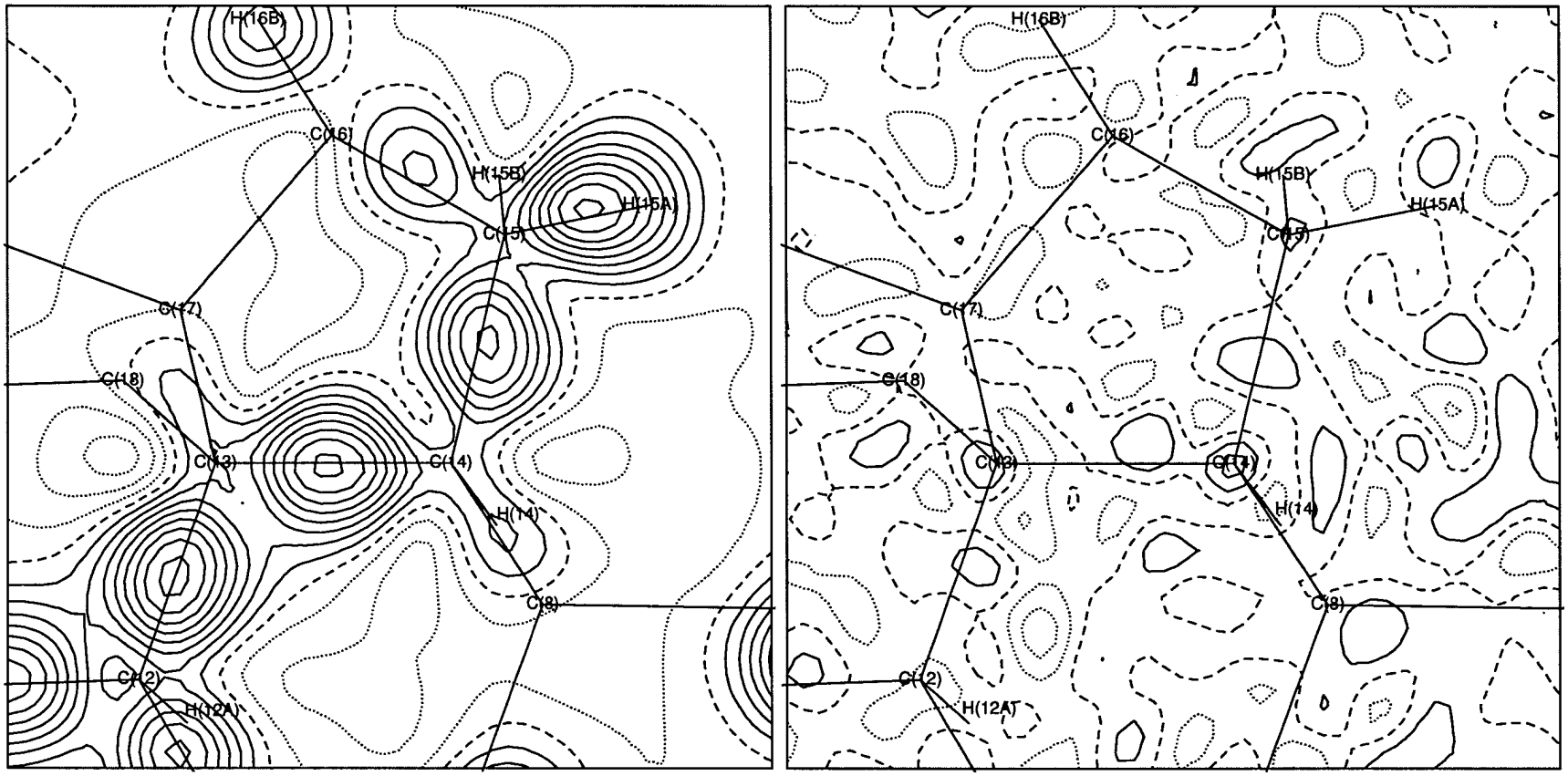

Figure B-4. Dynamic model map and residual map in the C13 – C14 – C15 plane of 17β-estradiol•urea. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

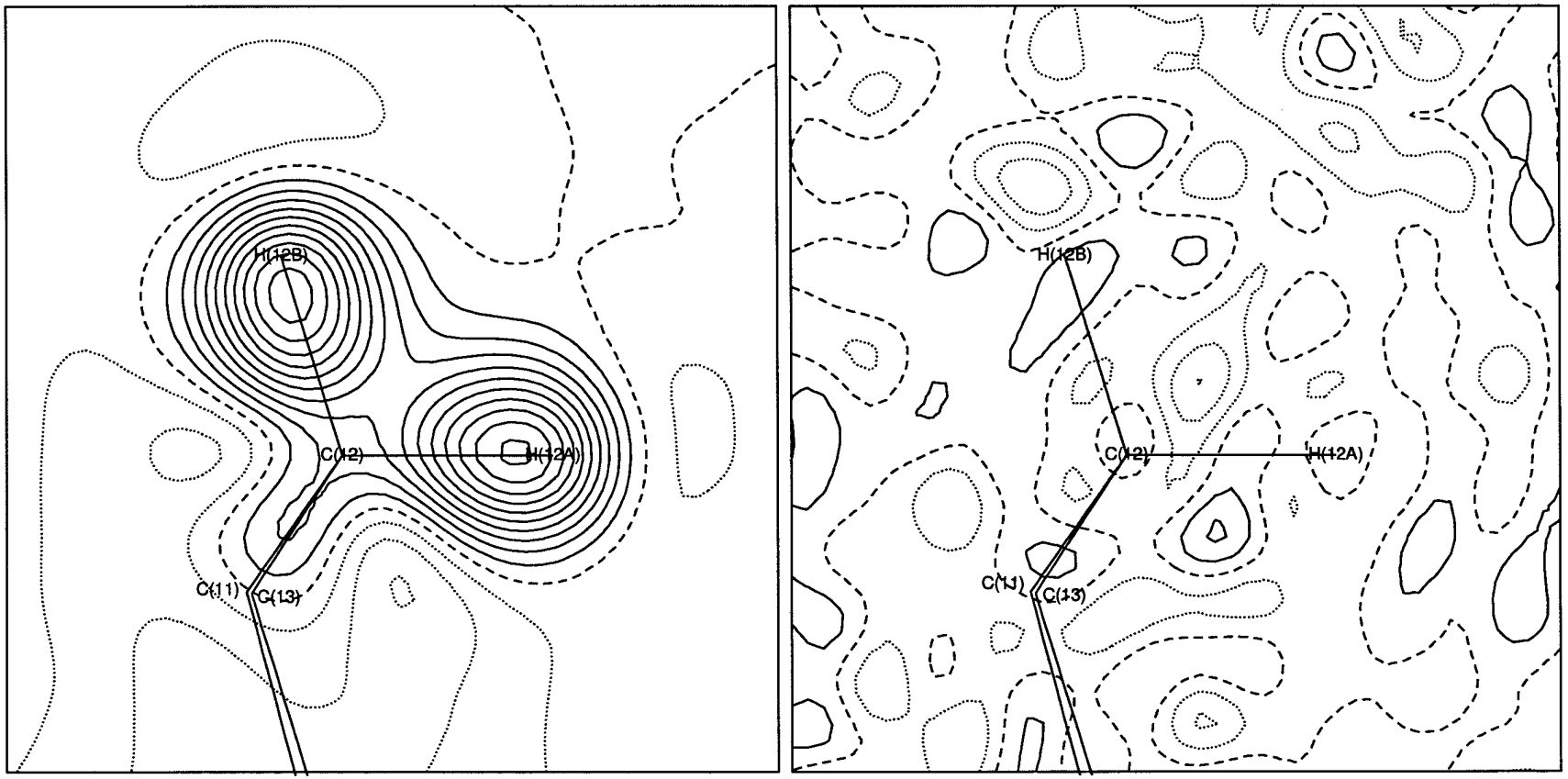

Figure B-5. Dynamic model map and residual map in the C12 – H12A – H12B plane of 17β-estradiol•urea. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

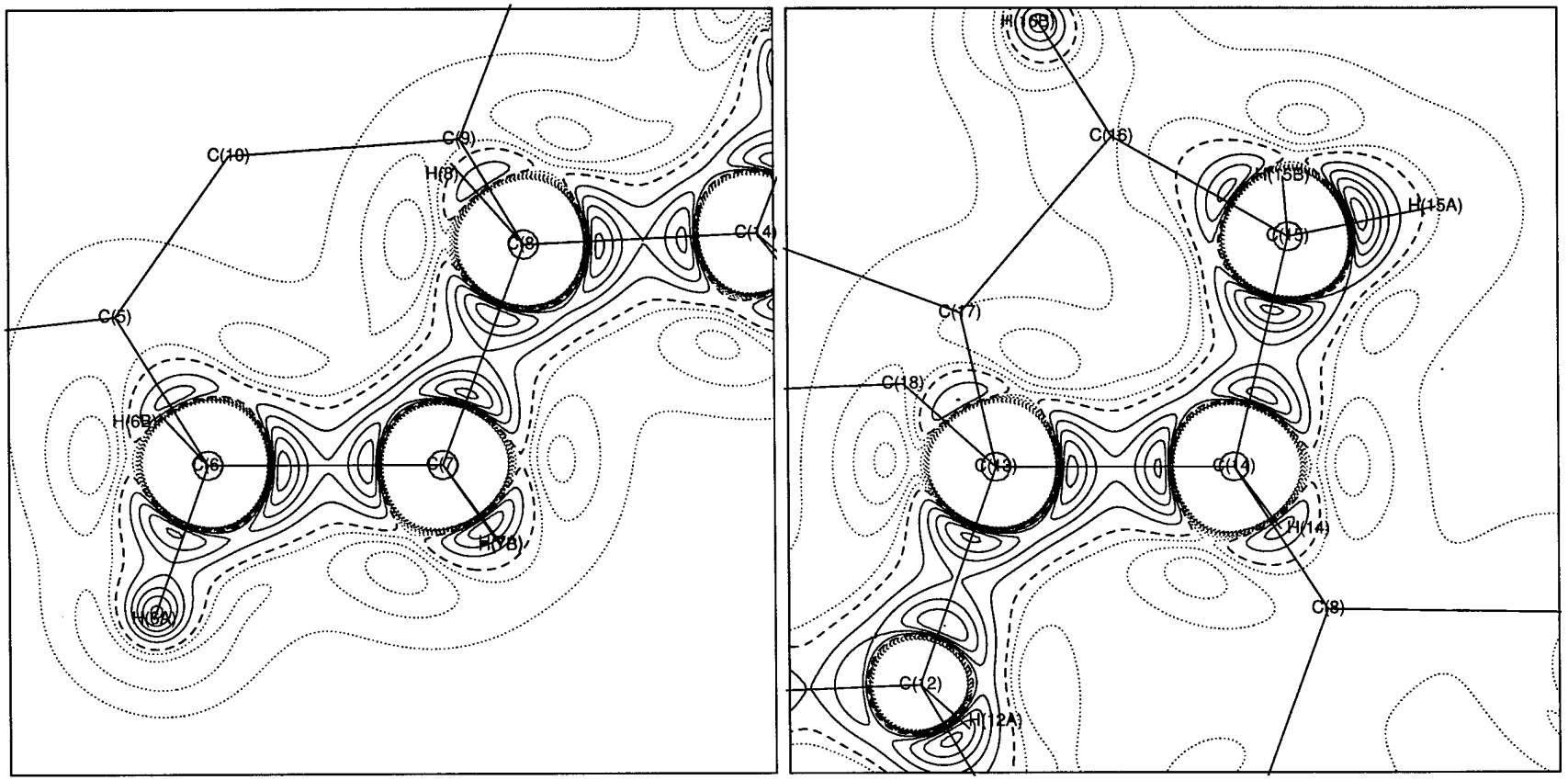

Figure B-6. The Laplacian of the total electron density of atoms at rest in the C6 – C7 – C8 and C13 – C14 – C15 planes of 17β-estradiol•urea. Contour intervals are 5 eÅ^{-5} starting at 5 eÅ^{-5} (solid blue lines), -2 eÅ^{-5} starting at -2 eÅ^{-5} (dotted red lines), and the dashed line equals 0 eÅ^{-5}.

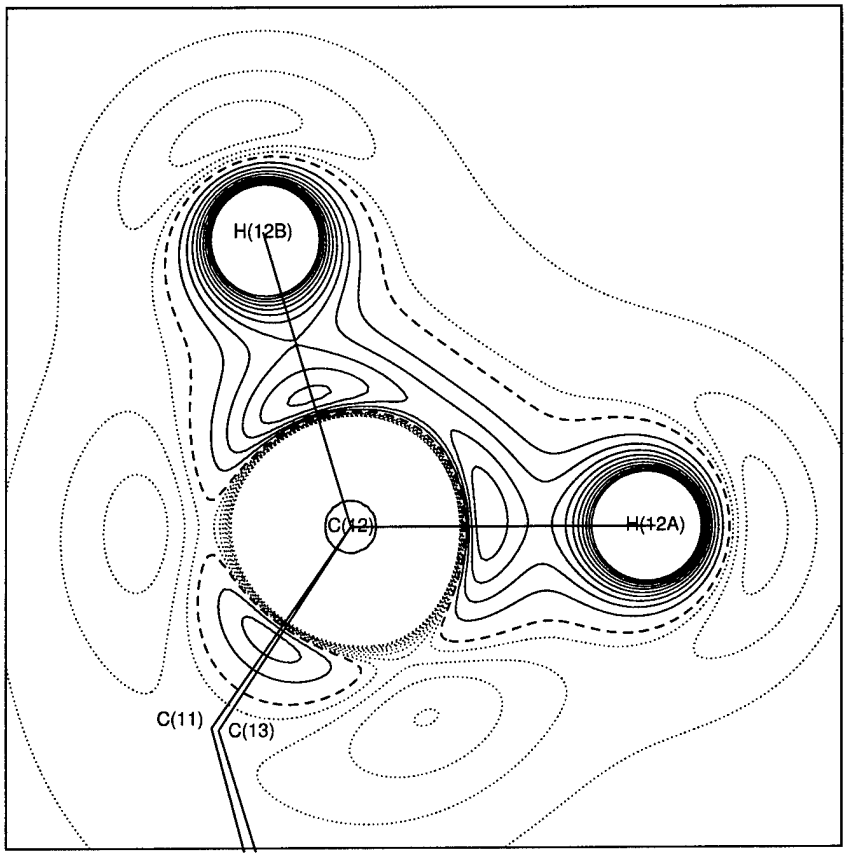

Figure B-7. The Laplacian of the total electron density of atoms at rest in the H12A – C12 – H12B plane of 17β-estradiol•urea. Contour intervals are 5 eÅ^{-5} starting at 5 eÅ^{-5} (solid blue lines), -2 eÅ^{-5} starting at -2 eÅ^{-5} (dotted red lines), and the dashed line plots 0 eÅ^{-5}.

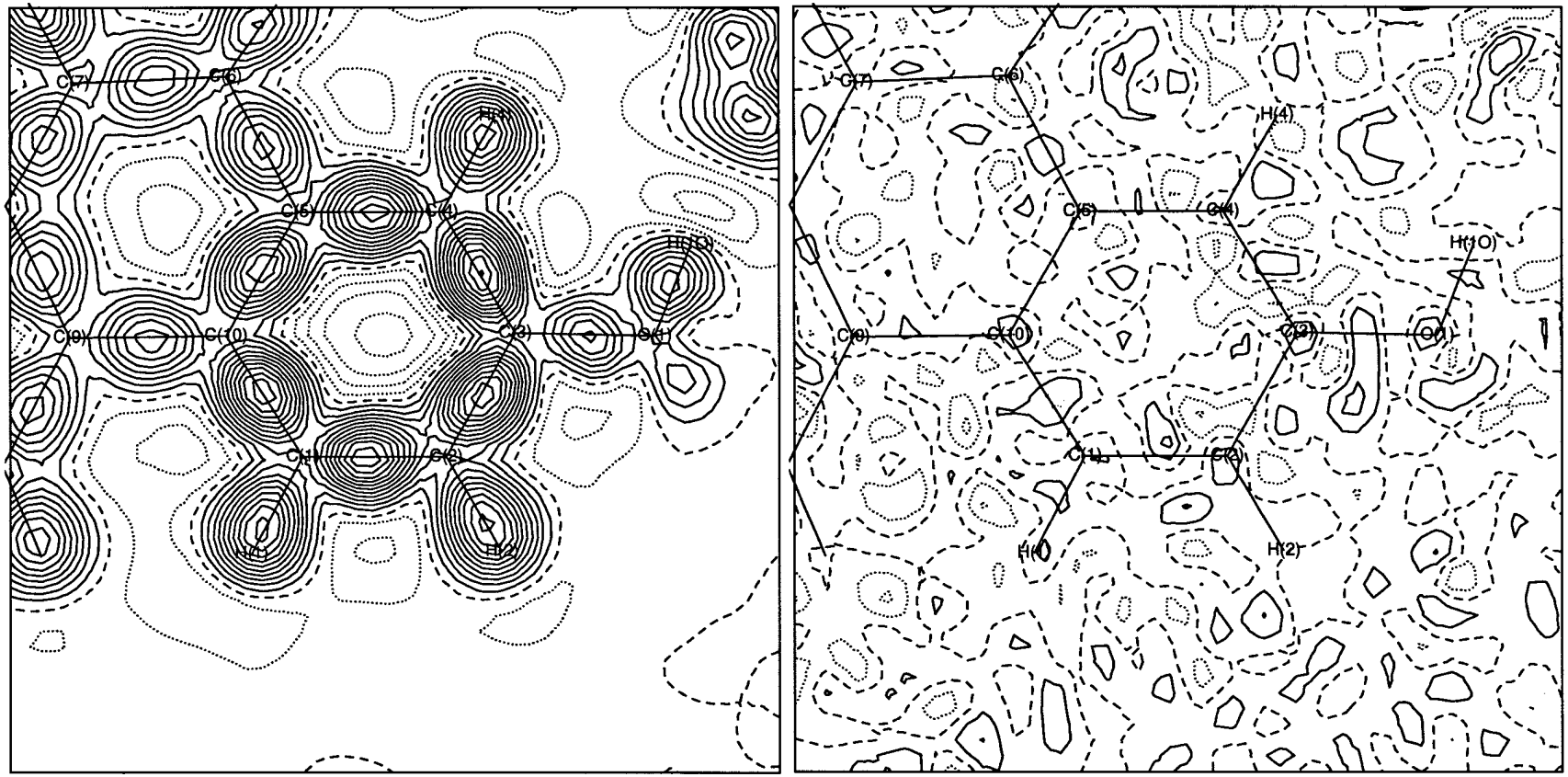

Figure B-8. Dynamic model map and residual map in the plane of the aromatic ring of 17β-estradiol•urea. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

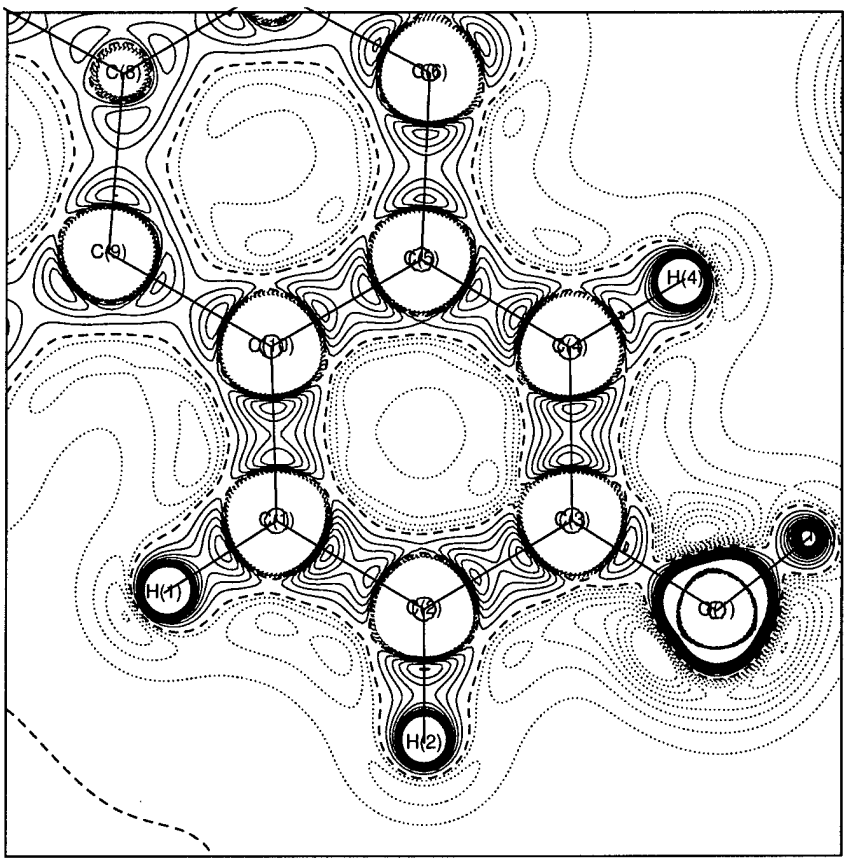

Figure B-9. The Laplacian of the total electron density of atoms at rest in the plane of the aromatic ring of 17β-estradiol•urea. Contour intervals are 5 eÅ^{-5} starting at 5 eÅ^{-5} (solid blue lines), -2 eÅ^{-5} starting at -2 eÅ^{-5} (dotted red lines), and the dashed line plots 0 eÅ^{-5}.

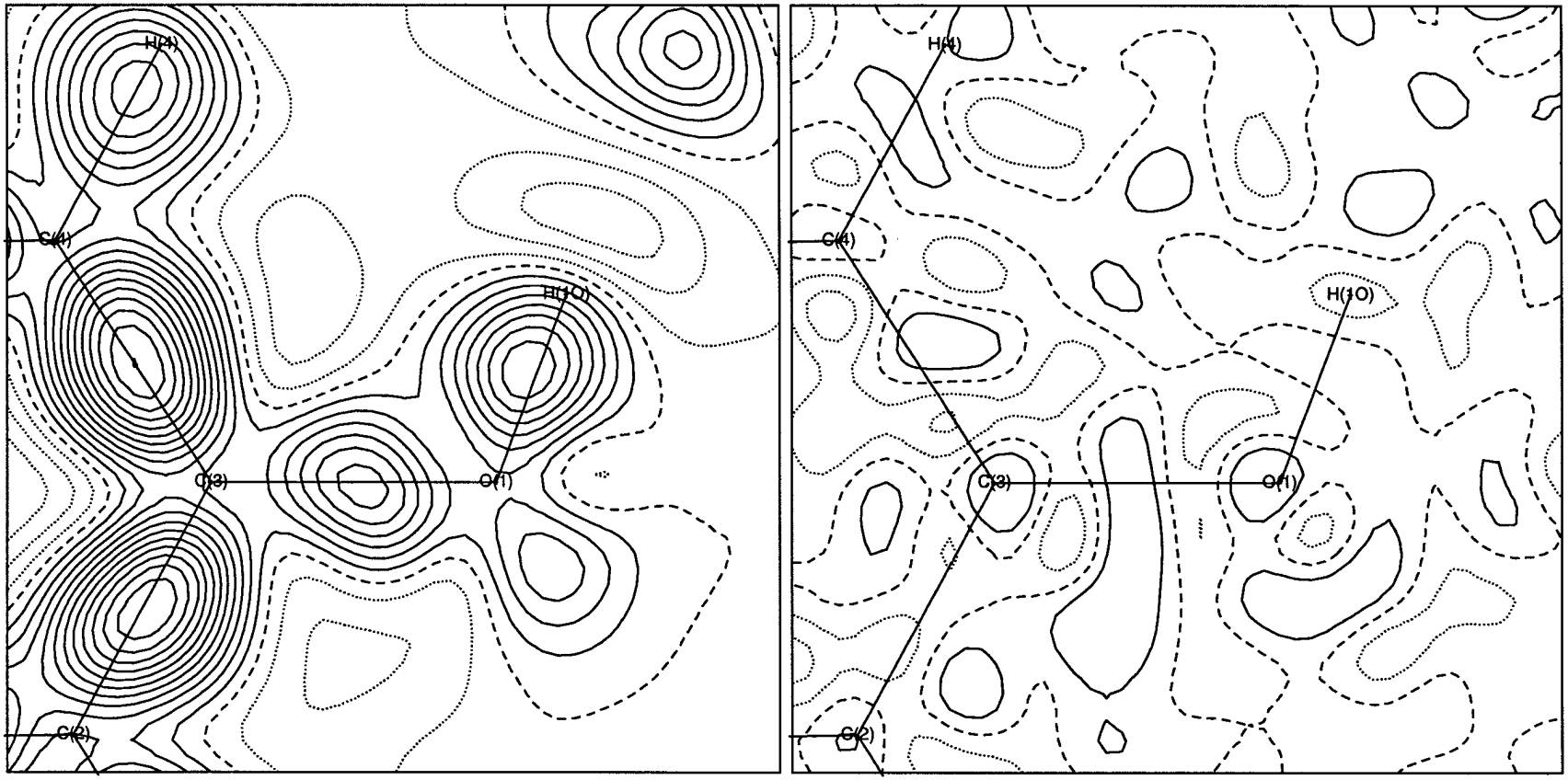

Figure B-10. Dynamic model map and residual map in the C3 – O1 – H1O plane of 17β-estradiol•urea. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

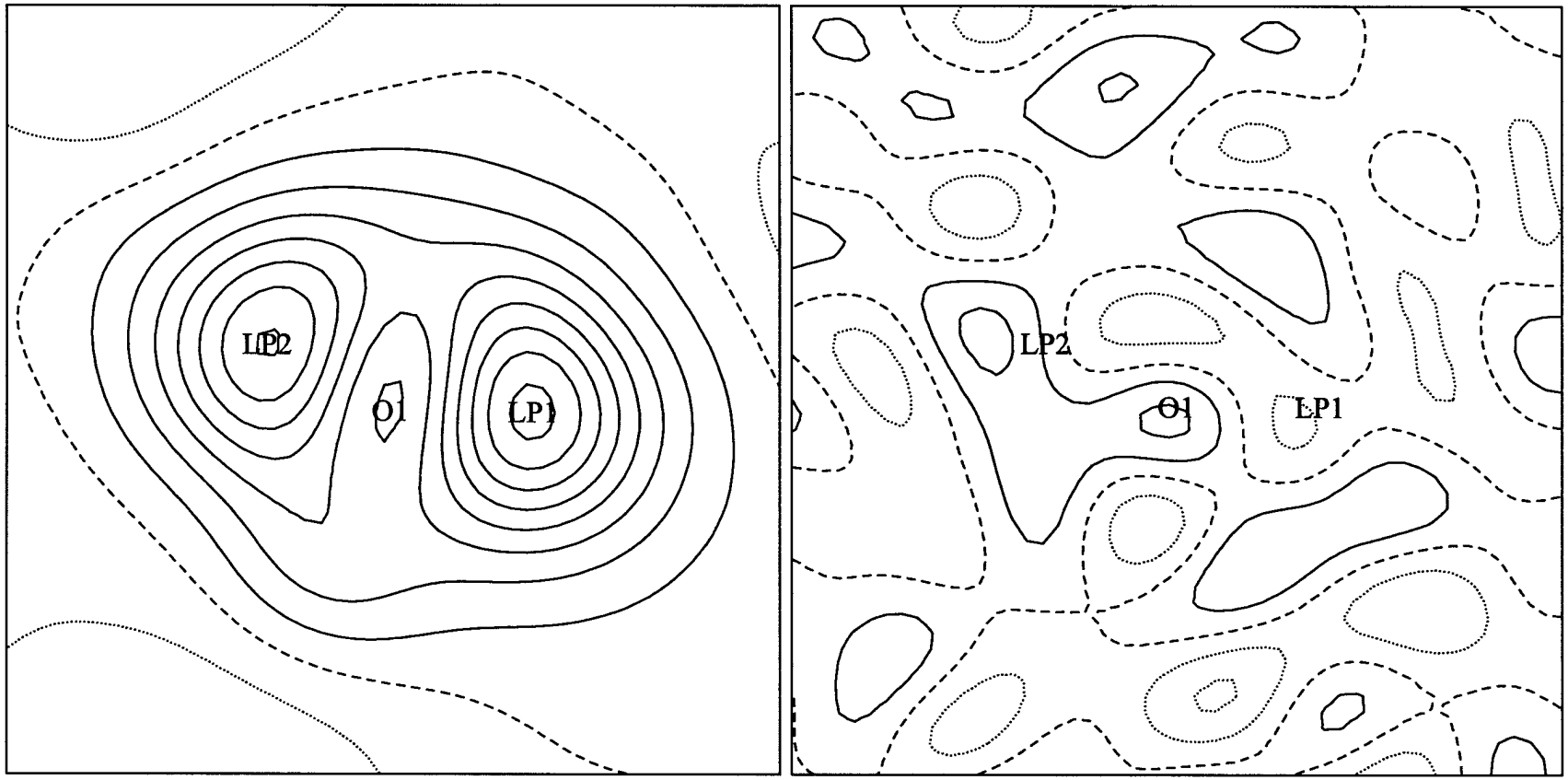

Figure B-11. Dynamic model map and residual map in the plane of the lone pairs of O1 of 17β-estradiol•urea. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

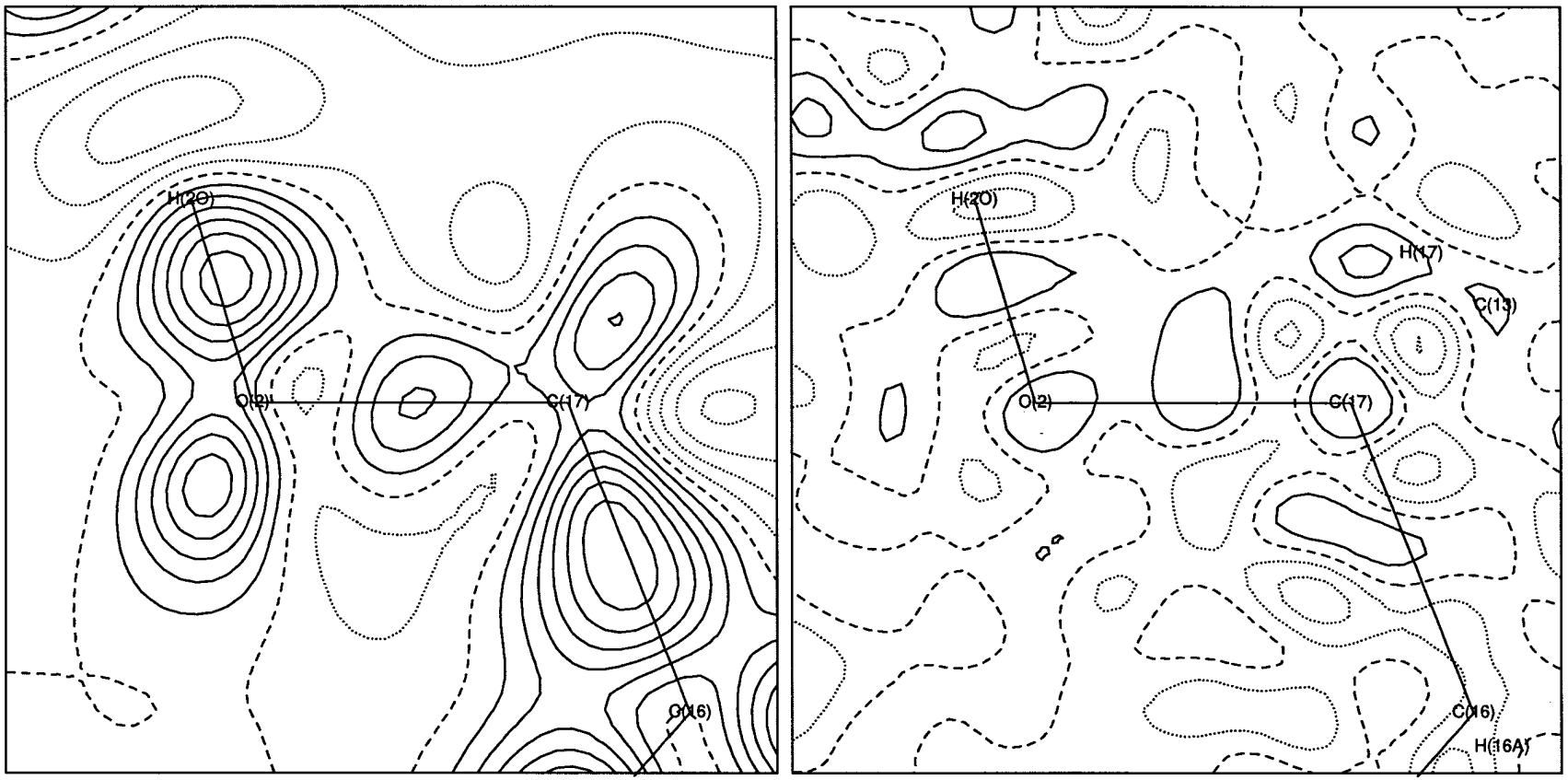

Figure B-12. Dynamic model map and residual map in the C17 – O2 – H2O plane of 17β-estradiol•urea. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

Figure B-13. Dynamic model map and residual map in the plane of the lone pairs of O2 of 17β-estradiol•urea. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

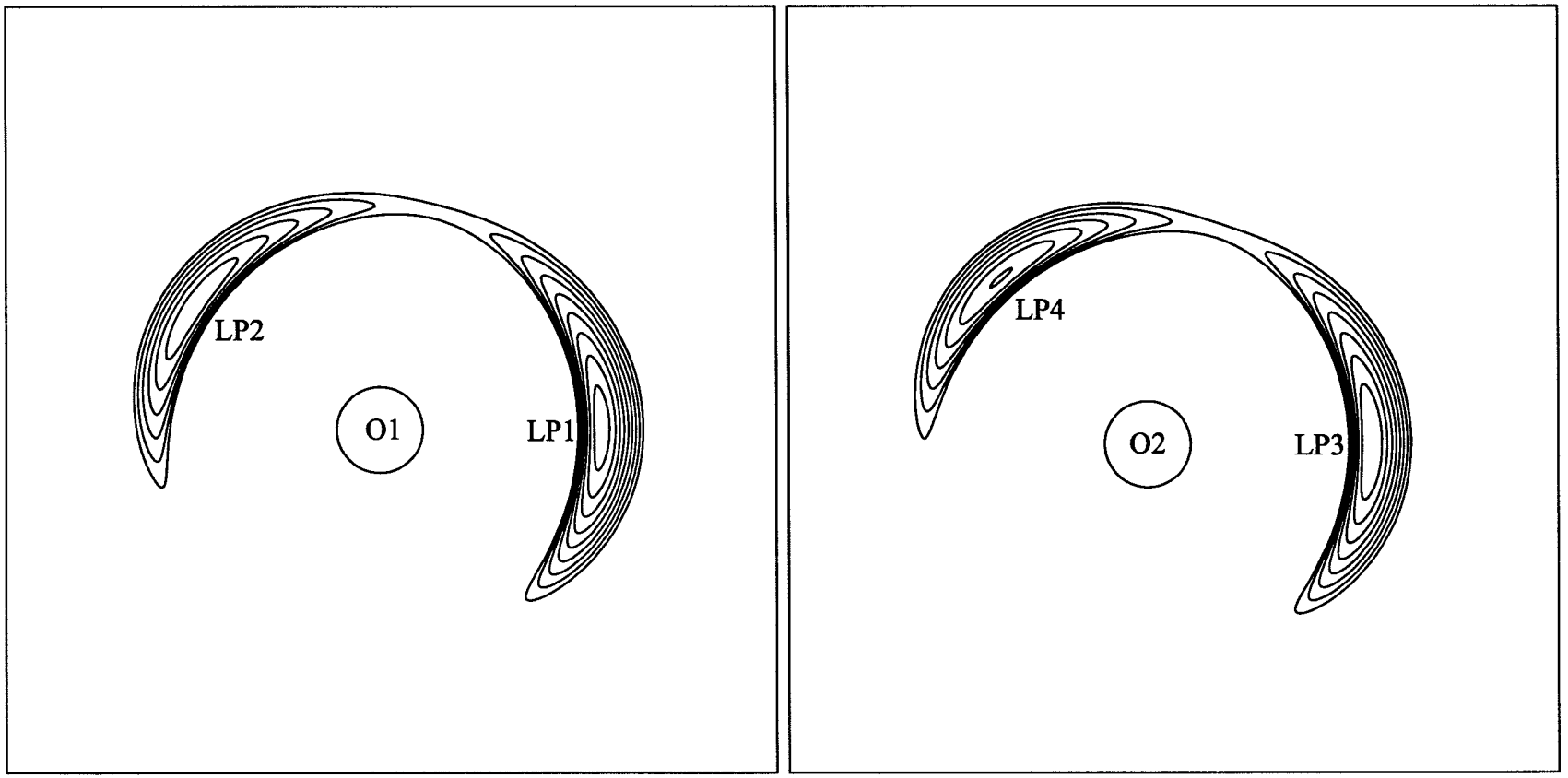

Figure B-14. The Laplacian of the total electron density of atoms at rest in the plane of the lone pairs of the oxygen atoms of 17β-estradiol•urea. Contour intervals are 5 eÅ^{-5} starting at 90 eÅ^{-5} for O1 and 80 eÅ^{-5} for O2.

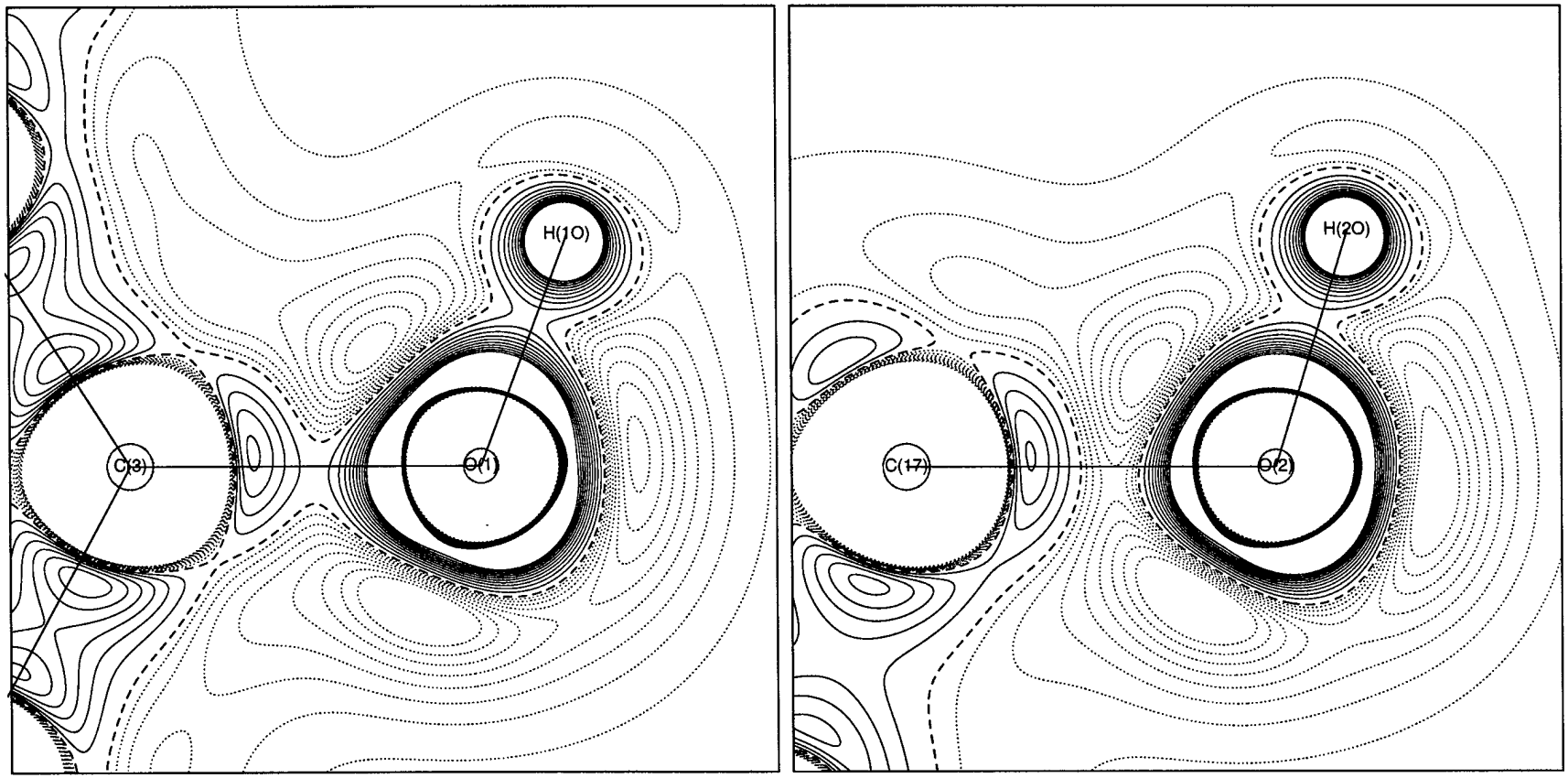

Figure B-15. The Laplacian of the total electron density of atoms at rest in the C3–O1–H1O plane and C17–O2–H2O of 17β-estradiol•urea. Contour intervals are 5 eÅ^{-5} starting at 5 eÅ^{-5} (solid blue lines), -2 eÅ^{-5} starting at -2 eÅ^{-5} (dotted red lines), and the dashed line plots 0 eÅ^{-5}.

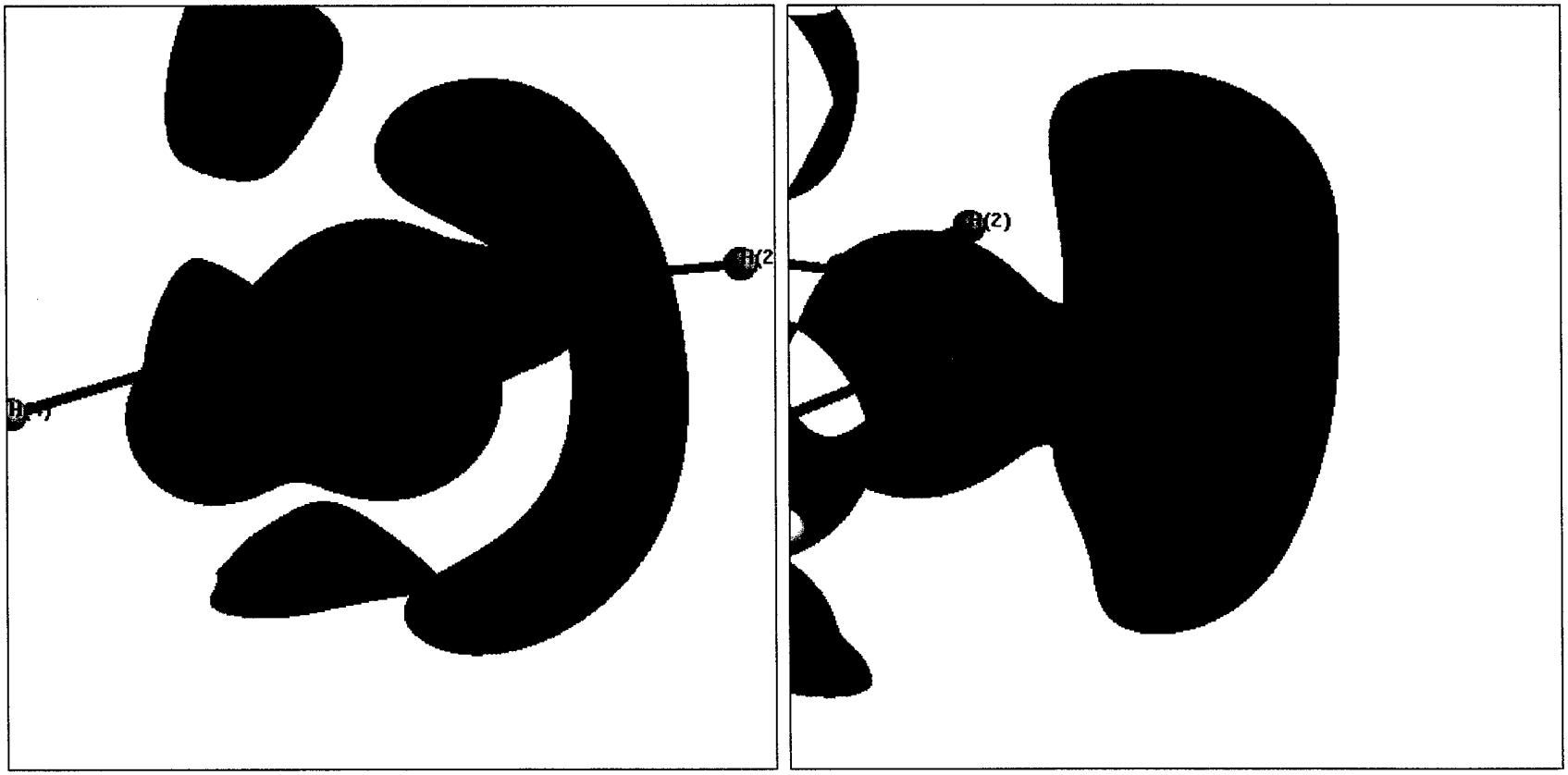

Figure B-16. 17β-estradiol•urea, C3 hydroxy, red –0.15 eÅ^{-1}, blue 1.0 eÅ^{-1}.

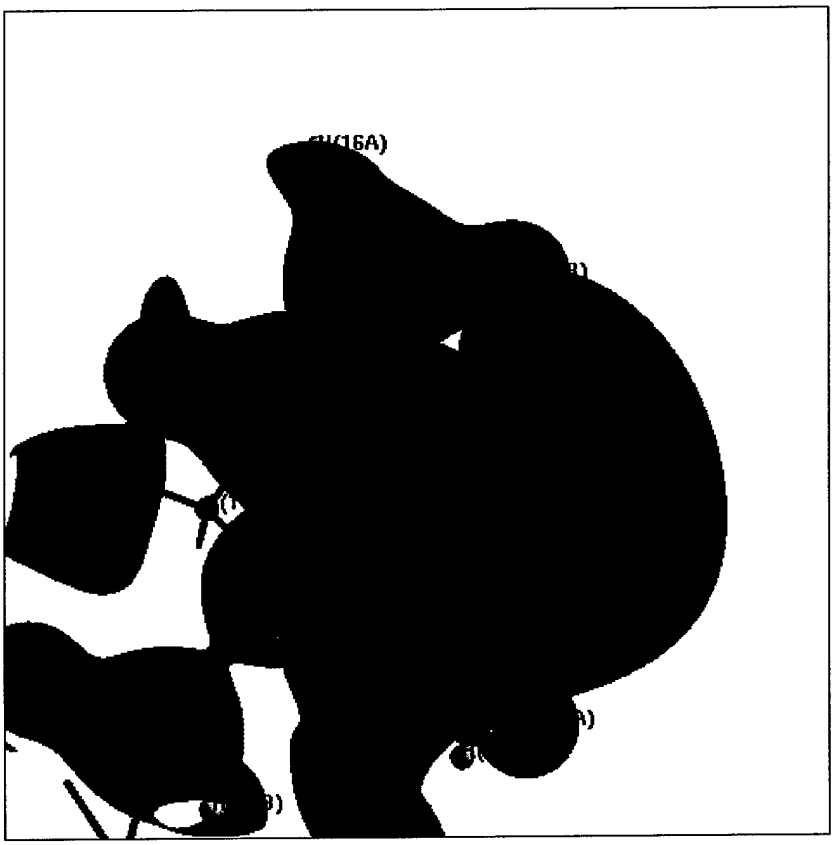

Figure B-17. 17β-estradiol•urea, C17 hydroxy, red –0.15 eÅ^{-1}, blue 1.0 eÅ^{-1}.

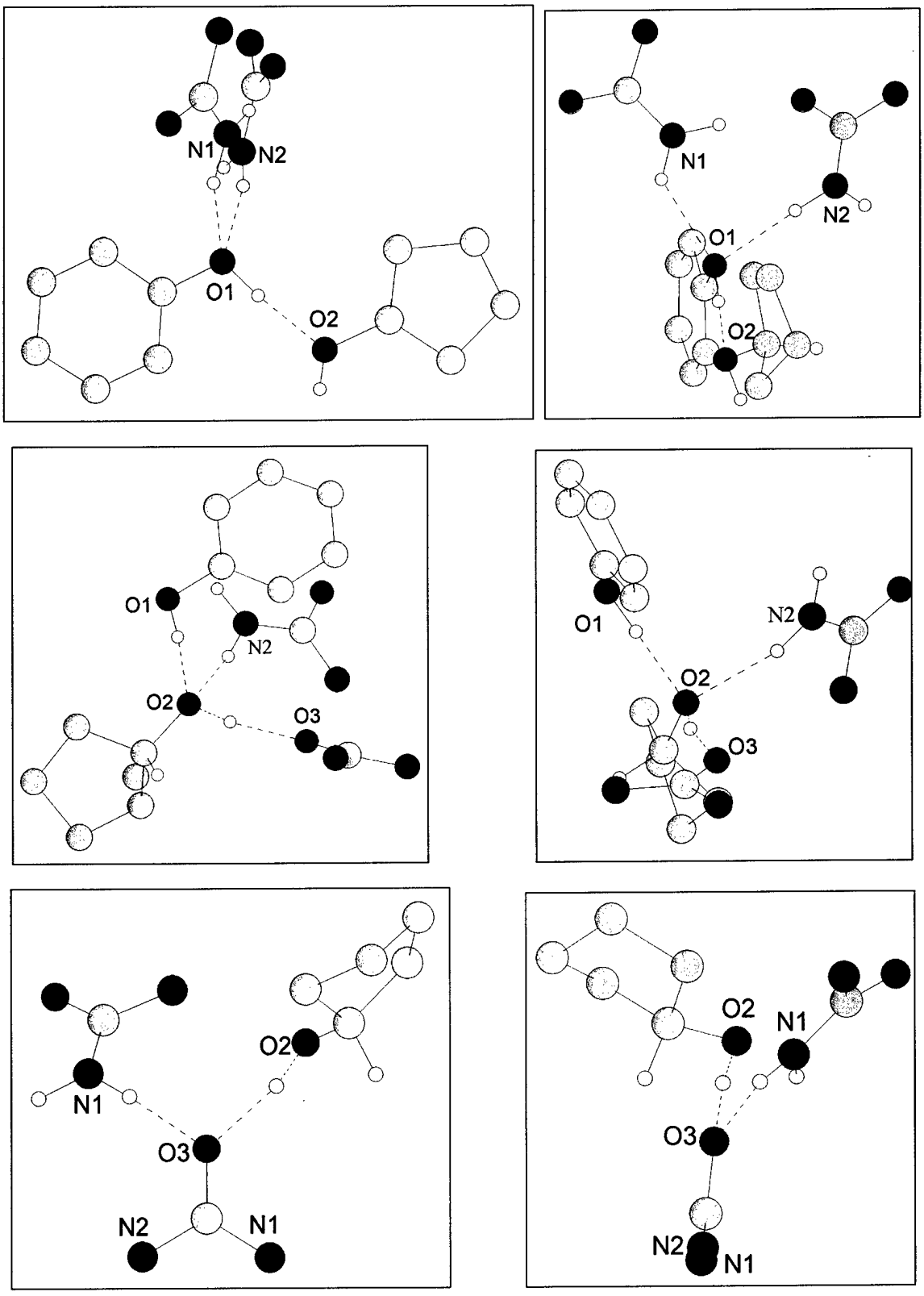

Figure B-18. Geometry of hydrogen bonding interactions of 17β-estradiol•urea.

Appendix C
17β-estradiol•½methanol

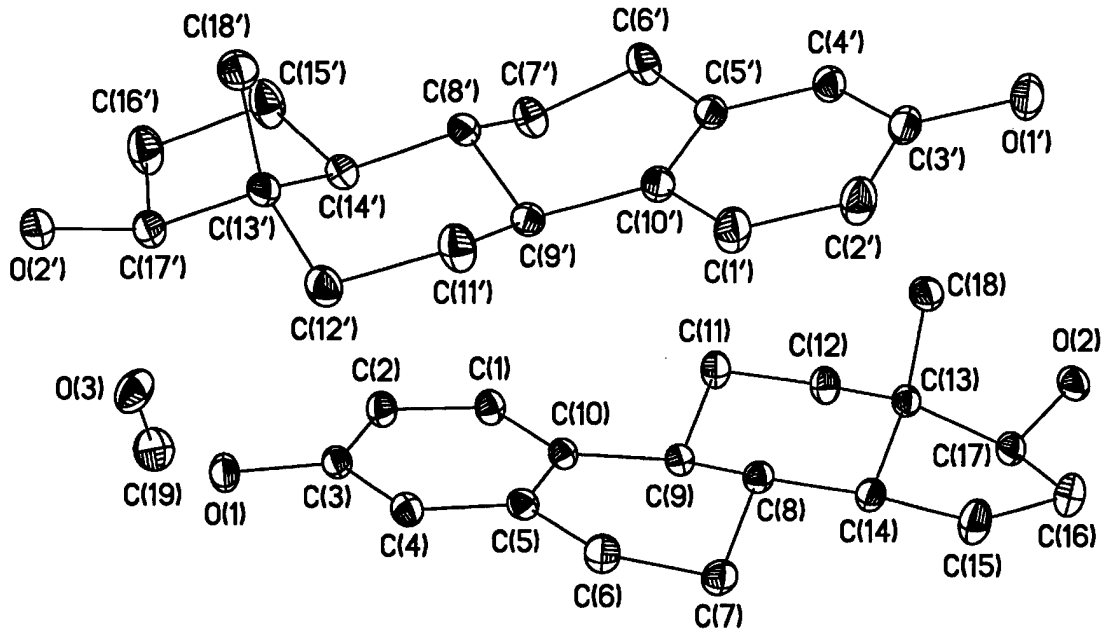

Figure C-1. Thermal ellipsoid plot of 17β-estradiol•½methanol where ellipsoids represent 50% probability electron density of the atom. Hydrogen atoms are omitted for clarity.

Run	2θ	ω	ϕ	Scan Width (°)	# of Frames	Frame Times (sec)
1	-40	-46	22	-0.15	1100	16
2	-40	-46	112	-0.15	1100	16
3	-40	-46	202	-0.15	1100	16
4	-40	-46	292	-0.15	1100	16
5	-80	-86	67	-0.15	1100	32
6	-80	-86	157	-0.15	1100	32
7	-80	-86	247	-0.15	1100	32
8	-80	-86	337	-0.15	1100	32
9	-102	-108	22	-0.15	1100	64
10	-102	-108	112	-0.15	1100	64
11	-102	-108	202	-0.15	1100	64
12	-102	-108	292	-0.15	1100	64

Table C-1. Data collection parameters for 17β-estradiol•½methanol.

Crystal Data			
Chemical Formula	$C_{37}H_{52}O_5$		
Temperature	100.0(1) K		
Crystal Dimensions	0.22 x 0.26 x 0.42 mm		
Space Group	P1		
A	7.2910(1) Å		
B	9.2768(1) Å		
C	12.3873(2) Å		
α	89.4704(6)		
β	87.8577(6)		
γ	70.7607(7)		
Volume	790.489(33) $Å^3$		
Z (Crystallographic)	2		
Integration Parameters			
	Box Size (°)	Profile Fitting (I/σ)	Simple Sum Perimeter Limit
Low Angle	1.5 x 1.5 x 1.0	20 20	0.02
Medium Angle	1.2 x 1.2 x 0.8	20 20	0.02
High Angle	1.0 x 1.0 x 0.6	10 10	0.02
Reflection Statistics (from SORTAV)			
Total Reflections	86369		
Rejected Outliers	33		
Unique Reflections	29051		
Average Redundancy	3.0		
Resolution	1.329 $Å^{-1}$		
Completeness	91.9 %		
R_1	5.77 %		
R_2	5.34 %		
R_w	15.25 %		
Z (Refinement)	1.219		

Table C-2. Selected crystal, integration, and reflection data for 17β-estradiol•½methanol.

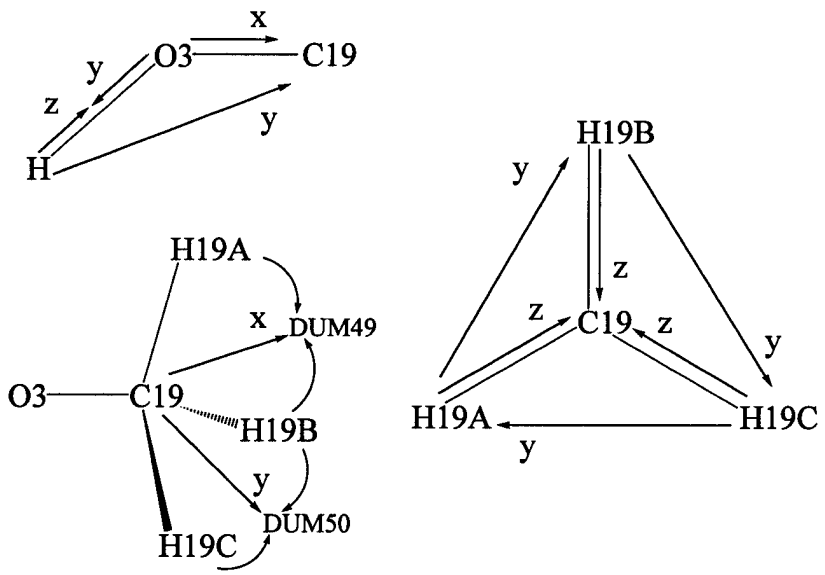

Figure C-2. Coordinate system for the methanol molecule.

	n	*m*	<*n*>	R_1	R_2	R_w	*Z*	*V*
Q < -4	0	0	0.0	0.0000	0.0000	0.0000	0.000	0.000
-4 < Q < -3	0	0	0.0	0.0000	0.0000	0.0000	0.000	0.000
-3 < Q < -2	8	4	2.0	0.3321	0.3844	0.3018	1.034	0.263
-2 < Q < -1	173	74	2.3	0.5492	0.6949	0.3870	0.761	0.455
-1 < Q < 0	2508	941	2.7	1.1243	1.1755	1.0245	1.183	2.153
0 < Q < 1	7959	2832	2.8	1.0254	1.0485	0.9274	1.329	1.501
1 < Q < 2	7845	2724	2.9	0.5759	0.6902	0.4618	1.252	0.519
2 < Q < 3	6736	2209	3.0	0.3661	0.4556	0.2863	1.194	0.322
3 < Q < 4	5725	1806	3.2	0.2602	0.3270	0.2132	1.220	0.235
4 < Q < 6	10058	2909	3.5	0.1800	0.2248	0.1548	1.231	0.170
6 < Q < 8	8497	2264	3.8	0.1266	0.1558	0.1169	1.254	0.127
8 < Q < 10	6921	1723	4.0	*0.0969*	0.1194	0.0927	1.242	0.101
10 < Q < 20	18395	4459	4.1	0.0596	0.0679	0.0645	1.224	0.063
20 < Q < 30	4702	1214	3.9	0.0389	0.0677	0.0370	1.193	0.040
30 < Q < 50	1174	361	3.3	0.0232	0.0273	0.0241	1.141	0.025
50 < Q < 100	212	75	2.8	0.0115	0.0136	0.0142	1.028	0.011
100 < Q	0	0	0.0	0.0000	0.0000	0.0000	0.000	0.000

Table C-3. Intensity-Significance Intervals where *n* is the number of reflections, *m* is the number of unique reflections, <*n*> is the average measurement multiplicity, and Q=I/Max ($\sigma_{int}/\sigma_{ext}$) respectively for 17$\beta$-estradiol•½methanol.

	n	*m*	<*n*>	R_1	R_2	R_w	*Z*	*V*
D > 1.016	4805	1570	3.1	.0345	.0529	.0721	1.568	.035
1.016 > D > 0.806	6705	1582	4.2	.0512	.0579	.0943	1.358	.057
0.806 > D > 0.705	6464	1594	4.1	.0554	.0578	.1004	1.337	.061
0.705 > D > 0.640	7744	1576	4.9	.0711	.0719	.1065	1.271	.075
0.640 > D > 0.594	8049	1558	5.2	.0792	.0777	.1080	1.250	.081
0.594 > D > 0.559	7545	1532	4.9	.1092	.1085	.1249	1.189	.105
0.559 > D > 0.531	6152	1521	4.0	.1373	.1371	.1424	1.155	.124
.531 > D > 0.508	4376	1441	3.0	.1334	.1241	.1677	1.274	.135
.508 > D > 0.488	4098	1401	2.9	.1508	.1428	.1755	1.245	.148
.488 > D > 0.472	4118	1436	2.9	.1593	.1445	.1895	1.280	.155
.472 > D > 0.457	3747	1354	2.8	.1854	.1681	.1988	1.230	.177
.457 > D > 0.444	3746	1387	2.7	.2289	.2205	.2122	1.192	.215
.444 > D > 0.432	3456	1331	2.6	.3003	.3007	.2497	1.183	.270
.432 > D > 0.422	3298	1303	2.5	.3737	.3823	.2719	1.167	.333
.422 > D > 0.412	2886	1194	2.4	.3703	.3773	.2801	1.166	.321
.412 > D > 0.403	1376	641	2.1	.3296	.3234	.3198	1.396	.309
.403 > D > 0.395	986	493	2.0	.3404	.3040	.3670	1.502	.352
.395 > D > 0.388	754	377	2.0	.4069	.3446	.4136	1.574	.431
.388 > D > 0.381	500	250	2.0	.4569	.4011	.4303	1.430	.486
.381 > D > 0.374	108	54	2.0	.5333	.4996	.5168	1.417	.584

Table C-4. Equal-Volume Resolution Shells where *n* is the number of reflections, *m* is the number of unique reflections, <*n*> is the average measurement multiplicity, and S=sinθ/λ ($Å^{-1}$) respectively for 17β-estradiol•½methanol.

	Monopole	sp^2		sp^3
		20	33+	32-
O1	-0.50			
O2	-0.49			
C1	-0.30	-0.22	0.34	
C2	-0.38	-0.19	0.37	
C3	0.27	-0.21	0.38	
C4	-0.33	-0.17	0.36	
C5	-0.18	-0.22	0.33	
C6	-0.26			0.31
C7	-0.31			0.34
C8	-0.21			0.39
C9	-0.17			0.31
C10	-0.25	-0.18	0.37	
C11	-0.31			0.35
C12	-0.28			0.31
C13	-0.16			0.38
C14	-0.20			0.38
C15	-0.26			0.33
C16	-0.35			0.42
C17	0.20			0.38
C18	-0.32			0.27

	Monopole
H1O	0.40
H2O	0.38
H1	0.23
H2	0.22
H4	0.26
H6x	0.20
H7x	0.17
H8	0.20
H9	0.16
H11x	0.17
H12x	0.16
H14	0.19
H15x	0.16
H16x	0.18
H17	0.13
H18x	0.18

Atoms	Kappa	κ	κ'
O1, O2, O3	1	0.97	1.16
C3	2	1.01	0.92
C17	3	1.02	0.95
C1, C2, C4	4	0.97	0.92
C5, C10	5	0.98	0.87
C6, C7, C8, C9, C11, C12, C13, C14, C15, C16, C17, C18, C19	6	0.98	0.95
all C-H hydrogen atoms	7	1.20	1.29
H1O, H2O, H3O	8	1.20	1.29

Table C-5. Starting values entered into the model for the multipole refinement for 17β-estradiol•½methanol. Units for multipole populations are e^-.

Atom	X	Y	Z
O1	0.08240(13)	0.21162(10)	0.936405(8)
O2	0.10594(13)	-0.05126(10)	0.06557(7)
C1	-0.06613(13)	0.15097(10)	0.66487(7)
C2	-0.08242(13)	0.19541(10)	0.77285(7)
C3	0.08629(14)	0.17723(11)	0.82894(7)
C4	0.26644(14)	0.12231(11)	0.77447(7)
C5	0.28180(13)	0.08148(10)	0.66531(7)
C6	0.48051(13)	0.03222(10)	0.60930(8)
C7	0.49100(12)	-0.05741(10)	0.50539(7)
C8	0.32007(13)	0.02383(10)	0.43507(7)
C9	0.12862(13)	0.02870(10)	0.49496(7)
C10	0.11375(14)	0.09174(11)	0.60917(7)
C11	-0.04837(13)	0.10675(10)	0.42644(7)
C12	-0.03113(14)	0.03067(11)	0.31502(7)
C13	0.15891(13)	0.02225(10)	0.25505(6)
C14	0.33043(13)	-0.05715(10)	0.32756(7)
C15	0.51074(13)	-0.08784(11)	0.25121(7)
C16	0.43778(12)	-0.11963(10)	0.14061(7)
C17	0.21795(13)	-0.09091(10)	0.15990(8)
C18	0.15271(14)	0.18231(10)	0.21808(7)

Atom	X	Y	Z
H1O	-0.0503(22)	0.2510(18)	0.9652(12)
H2O	0.1284(24)	0.0361(18)	0.0311(12)
H1	-0.2009(20)	0.1644(16)	0.6260(11)
H2	-0.2242(21)	0.2411(16)	0.8125(11)
H4	0.3944(20)	0.1116(16)	0.8194(10)
H6A	0.5897(19)	-0.0323(15)	0.6651(11)
H6B	0.5127(20)	0.1370(16)	0.5919(11)
H7A	0.4844(20)	-0.1709(16)	0.5233(11)
H7B	0.6269(20)	-0.0687(15)	0.4609(11)
H8	0.3190(21)	0.1410(16)	0.4195(11)
H9	0.1338(19)	-0.0908(15)	0.5028(10)
H11A	-0.1825(20)	0.1042(16)	0.4670(11)
H11B	-0.0617(20)	0.2269(16)	0.4192(11)
H12A	-0.0363(20)	-0.0845(16)	0.3270(11)
H12B	-0.1555(20)	0.0952(15)	0.2685(11)
H14	0.3164(20)	-0.1689(16)	0.3477(11)
H15A	0.6267(22)	-0.1869(17)	0.2797(12)
H15B	0.5532(22)	0.0144(17)	0.2507(12)
H16A	0.5101(21)	-0.2360(16)	0.1119(11)
H16B	0.4559(22)	-0.0401(17)	0.0791(12)
H17	0.1966(20)	-0.1975(15)	0.1875(11)
H18A	0.0354(21)	0.2267(16)	0.1658(11)
H18B	0.1336(20)	0.2577(16)	0.2845(11)
H18C	0.2817(22)	0.1811(17)	0.1751(12)

Table C-6. Fractional atomic coordinates for molecule 1 of 17β-estradiol•½methanol.

Atom	X	Y	Z
O1'	0.44563(13)	0.49573(10)	0.14404(8)
O2'	0.15712(13)	0.64715(11)	1.02254(7)
C1'	0.50368(13)	0.44528(10)	0.43452(7)
C2'	0.54823(14)	0.44473(10)	0.32415(8)
C3'	0.39817(13)	0.49586(10)	0.25199(7)
C4'	0.20597(13)	0.54530(10)	0.29149(7)
C5'	0.16168(13)	0.54570(11)	0.40252(7)
C6'	-0.05026(14)	0.60488(10)	0.43907(7)
C7'	-0.08644(13)	0.56878(10)	0.55668(8)
C8'	0.06136(13)	0.60192(10)	0.62803(7)
C9'	0.26559(13)	0.49008(11)	0.59721(7)
C10'	0.31159(13)	0.49584(10)	0.47642(7)
C11'	0.42220(13)	0.51079(10)	0.66974(7)
C12'	0.37063(14)	0.50141(10)	0.79075(8)
C13'	0.17009(14)	0.61553(11)	0.82063(7)
C14'	0.01990(13)	0.58481(10)	0.74798(7)
C15'	-0.17643(13)	0.68090(10)	0.79979(7)
C16'	-0.13940(13)	0.66862(10)	0.92246(7)
C17'	0.08319(13)	0.59214(11)	0.93220(7)
C18'	0.17533(13)	0.77899(10)	0.81232(8)
O3	-0.28167(13)	0.29338(10)	1.01529(7)
C19	-0.35895(13)	0.17109(11)	1.02075(7)
H3O	-0.35307(25)	0.37300(22)	1.06225(17)
H19A	-0.29199(24)	0.08909(21)	0.95875(15)
H19B	-0.51182(24)	0.21209(20)	1.00791(15)
H19C	-0.34233(23)	0.11940(20)	1.09895(15)

Atom	X	Y	Z
H1O'	0.3341(22)	0.5447(17)	0.1007(12)
H2O'	0.1344 (23)	0.7561(17)	1.0186(12)
H1'	0.6239 (21)	0.4062(16)	0.4879(11)
H2'	0.6958(21)	0.4029(16)	0.2915(11)
H4'	0.0906(20)	0.5827(15)	0.2349(11)
H6C	-0.1306(20)	0.5579(15)	0.3848(11)
H6D	-0.1013(21)	0.7288(17)	0.4312(12)
H7C	-0.0741(20)	0.4489(16)	0.5651(11)
H7D	-0.2360(19)	0.6359(15)	0.5793(10)
H8'	0.0560(19)	0.7196(15)	0.6101(10)
H9'	0.2574(20)	0.3759(16)	0.6148(11)
H11C	0.5588(21)	0.4192(17)	0.6528(11)
H11D	0.4370(20)	0.6218(16)	0.6521(11)
H12C	0.3708 (21)	0.3860(16)	0.8082(11)
H12D	0.4841(20)	0.5202(16)	0.8379(11)
H14'	0.0331(20)	0.4644(16)	0.7608(11)
H15C	-0.2902(21)	0.6352(16)	0.7785(11)
H15D	-0.2110(22)	0.8005(17)	0.7772(12)
H16C	-0.2159(21)	0.6001(17)	0.9642(12)
H16D	-0.1856(22)	0.7791(17)	0.9632(13)
H17'	0.1173(20)	0.4698(15)	0.9497(10)
H18D	0.2891(21)	0.7876(16)	0.8599(11)
H18E	0.2046(20)	0.8088(16)	0.7323(11)
H18F	0.0440(23)	0.8618(18)	0.8405(12)

Table C-7. Fractional atomic coordinates for molecule 2 and methanol of 17β-estradiol•½methanol.

Atom	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.02315(12)	0.01838(11)	0.01172(8)	-0.00821(9)	0.00038(8)	-0.00143(7)
O2	0.02742(14)	0.01660(10)	0.01237(8)	-0.00827(10)	-0.00257(8)	-0.00055(7)
C1	0.01183(10)	0.02079(13)	0.01240(9)	-0.00540(9)	0.00016(8)	-0.00046(9)
C2	0.01489(11)	0.01999(13)	0.01241(10)	-0.00567(10)	0.00116(8)	-0.00063(9)
C3	0.01715(12)	0.01344(10)	0.01130(9)	-0.00612(9)	-0.00016(8)	0.00036(8)
C4	0.01523(11)	0.01497(11)	0.01220(9)	-0.00595(9)	-0.00180(8)	0.00039(8)
C5	0.01212(10)	0.01365(10)	0.01193(9)	-0.00438(8)	-0.00169(8)	0.00091(8)
C6	0.01108(10)	0.02189(14)	0.01563(11)	-0.00391(10)	-0.00226(8)	-0.00091(10)
C7	0.01153(10)	0.01874(13)	0.01690(11)	-0.00068(9)	-0.00173(9)	-0.00146(10)
C8	0.01108(9)	0.01379(10)	0.01239(9)	-0.00381(8)	-0.00023(7)	-0.00045(8)
C9	0.01150(10)	0.01434(11)	0.01169(9)	-0.00501(8)	-0.00072(7)	0.00044(8)
C10	0.01091(9)	0.01456(11)	0.01085(9)	-0.00475(8)	-0.00064(7)	0.00068(8)
C11	0.01118(10)	0.02348(15)	0.01289(10)	-0.00428(10)	-0.00113(8)	-0.00183(9)
C12	0.01433(11)	0.02257(15)	0.01333(10)	-0.00799(10)	-0.00128(8)	-0.00153(9)
C13	0.01540(11)	0.01279(10)	0.01145(9)	-0.00557(9)	-0.00003(8)	-0.00079(7)
C14	0.01351(10)	0.01445(11)	0.01285(9)	-0.00400(9)	0.00044(8)	-0.00125(8)
C15	0.01524(13)	0.02956(19)	0.01735(13)	-0.00556(13)	0.00290(10)	-0.00514(12)
C16	0.02131(15)	0.02492(17)	0.01594(12)	-0.00703(13)	0.00430(11)	-0.00569(11)
C17	0.02088(13)	0.01382(11)	0.01227(10)	-0.00648(15)	-0.00006(11)	-0.00162(13)
C18	0.02731(16)	0.01397(12)	0.01504(11)	-0.00815(11)	-0.00065(11)	0.00034(9)
O1'	0.02050(12)	0.02548(14)	0.01264(9)	-0.00112(10)	0.00182(8)	-0.00266(9)
O2'	0.02908(14)	0.01675(10)	0.01253(8)	-0.00712(10)	-0.00434(9)	-0.00013(7)
C1'	0.01201(11)	0.02698(17)	0.01402(11)	0.00007(11)	-0.00084(13)	-0.00137(10)
C2'	0.01366(12)	0.02877(18)	0.01463(11)	-0.00027(11)	0.00023(9)	-0.00244(11)
C3'	0.01544(12)	0.01728(12)	0.01231(10)	-0.00199(10)	0.00038(9)	-0.00223(9)
C4'	0.01434(11)	0.01596(11)	0.01173(9)	-0.00340(9)	-0.00136(8)	-0.00047(8)
C5'	0.01218(10)	0.01417(10)	0.01179(9)	-0.00328(8)	-0.00185(8)	0.00034(8)
C6'	0.01206(11)	0.02589(16)	0.01333(10)	-0.00459(10)	-0.00254(8)	0.00307(10)
C7'	0.01301(11)	0.02461(15)	0.01363(10)	-0.00787(10)	-0.00229(8)	0.00273(10)
C8'	0.01167(9)	0.01277(10)	0.01186(9)	-0.00365(8)	-0.00136(7)	0.00172(7)
C9'	0.01227(10)	0.01343(10)	0.01241(9)	-0.00207(8)	-0.00242(8)	0.00063(8)
C10'	0.01146(10)	0.01537(11)	0.01218(9)	-0.00169(8)	-0.00187(8)	-0.00036(8)
C11'	0.01272(11)	0.02953(18)	0.01384(11)	-0.00590(12)	-0.00282(9)	0.00010(11)
C12'	0.01563(12)	0.02041(14)	0.01340(10)	-0.00364(11)	-0.00403(10)	0.00092(9)
C13'	0.01718(11)	0.01090(9)	0.01195(9)	-0.00572(9)	-0.00183(8)	0.00114(7)
C14'	0.01426(11)	0.01539(11)	0.01184(9)	-0.00583(9)	-0.00107(8)	0.00163(8)
C15'	0.01570(13)	0.03738(24)	0.01515(12)	-0.00321(14)	0.00057(10)	0.00073(13)
C16'	0.02051(15)	0.03456(22)	0.01457(12)	-0.00670(15)	0.00243(11)	-0.00056(13)
C17'	0.02185(14)	0.01486(11)	0.01165(9)	-0.00722(10)	-0.00124(9)	0.00096(8)
C18'	0.03705(22)	0.01437(12)	0.01709(12)	-0.01337(14)	-0.00299(13)	0.00180(10)
O3	0.02682(15)	0.02440(15)	0.02598(14)	-0.00745(12)	0.01130(12)	-0.00554(12)
C19	0.02730(20)	0.03127(23)	0.02636(19)	-0.01196(18)	0.00339(15)	0.00142(16)

Table C-8. Anisotropic thermal parameters of non-H atoms for 17β-estradiol•½methanol.

Atom	U_{iso}
H1O	0.0320(26)
H2O	0.0353(29)
H1	0.0453(25)
H2	0.0460(26)
H4	0.0429(24)
H6A	0.0404(21)
H6B	0.0491(26)
H7A	0.0495(25)
H7B	0.0475(24)
H8	0.0457(24)
H9	0.0386(21)
H11A	0.0488(25)
H11B	0.0493(25)
H12A	0.0519(26)
H12B	0.0462(24)
H14	0.0414(22)
H15A	0.0601(29)
H15B	0.0558(28)
H16A	0.0592(28)
H16B	0.0602(29)
H17	0.0505(23)
H18A	0.0572(27)
H18B	0.0554(26)
H18C	0.0658(31)

Atom	U_{iso}
H1O'	0.0326(27)
H2O'	0.0316(26)
H1'	0.0470(24)
H2'	0.0495(26)
H4'	0.0393(22)
H6C	0.0478(24)
H6D	0.0580(29)
H7C	0.0512(26)
H7D	0.0428(22)
H8'	0.0422(23)
H9'	0.0479(25)
H11C	0.0550(28)
H11D	0.0519(26)
H12C	0.0515(26)
H12D	0.0505(25)
H14'	0.0450(23)
H15C	0.0578(29)
H15D	0.0600(30)
H16C	0.0636(31)
H16D	0.0657(31)
H17'	0.0553(24)
H18D	0.0590(28)
H18E	0.0611(29)
H18F	0.0749(36)

H3O	0.0402(30)
H19A	0.0770(36)
H19B	0.0837(40)
H19C	0.0903(43)

Table C-9. Isotropic thermal parameters of H atoms for 17β-estradiol•½methanol.

Atoms	Bond Length (Å)
O1 – C3	1.3688(4)
O2 – C17	1.4259(5)
C1 – C2	1.3926(5)
C1 – C10	1.4009(4)
C2 – C3	1.3961(5)
C3 – C4	1.3925(5)
C4 – C5	1.3981(5)
C5 – C6	1.5111(5)
C5 – C10	1.4069(4)
C6 – C7	1.5247(5)
C7 – C8	1.5264(5)
C8 – C9	1.5435(4)
C8 – C14	1.5222(5)
C9 – C10	1.5223(5)
C9 – C11	1.5377(5)
C11 – C12	1.5381(5)
C12 – C13	1.5266(5)
C13 – C14	1.5421(5)
C13 – C17	1.5374(5)
C13 – C18	1.5366(5)
C14 – C15	1.5392(5)
C15 – C16	1.5532(6)
C16 – C17	1.5453(6)

Atoms	Bond Length (Å)
O1' – C3'	1.3687(4)
O2' – C17'	1.4284(5)
C1' – C2'	1.3930(5)
C1' – C10'	1.4029(5)
C2' – C3'	1.3944(5)
C3' – C4'	1.3938(5)
C4' – C5'	1.4007(4)
C5' – C6'	1.5124(5)
C5' – C10'	1.4073(4)
C6' – C7'	1.5247(5)
C7' – C8'	1.5270(5)
C8' – C9'	1.5447(4)
C8' – C14'	1.5225(4)
C9' – C10'	1.5254(4)
C9' – C11'	1.5404(5)
C11' – C12'	1.5405(5)
C12' – C13'	1.5304(5)
C13' – C14'	1.5408(5)
C13' – C17'	1.5421(5)
C13' – C18'	1.5319(5)
C14' – C15'	1.5351(5)
C15' – C16'	1.5499(6)
C16' – C17'	1.5511(6)

O3 – C19	1.4234(8)

Table C-10. Bond distances of non-H atoms of 17β-estradiol•½methanol.

Atoms	Bond Angle (°)
C3 – O1 – H1O	110.8(8)
C17 – O2 – H2O	109.5(8)
C2 – C1 – C10	122.4(1)
C2 – C1 – H1	116.1(6)
C10 – C1 – H1	121.4(6)
C1 – C2 – C3	119.1(1)
C1 – C2 – H2	119.9(6)
C3 – C2 – H2	120.9(6)
O1 – C3 – C2	122.5(1)
O1 – C3 – C4	118.1(1)
C2 – C3 – C4	119.4(1)
C3 – C4 – C5	121.2(1)
C3 – C4 – H4	117.9(6)
C5 – C4 – H4	120.9(6)
C4 – C5 – C6	118.5(1)
C4 – C5 – C10	120.0(1)
C6 – C5 – C10	121.5(1)
C5 – C6 - C7	113.4(1)
C5 – C6 – H6A	109.9(6)
C5 – C6 – H6B	105.9(6)
C7 – C6 – H6A	111.1(6)
C7 – C6 – H6B	110.2(6)
H6A – C6 – H6B	106.1(9)
C6 – C7 – C8	110.5(1)
C6 – C7 – H7A	110.7(6)
C6 – C7 – H7B	109.5(6)
C8 – C7 – H7A	107.7(6)
C8 – C7 – H7B	109.4(6)
H7A – C7 – H7B	109.0(8)
C7 – C8 – C9	109.3(1)
C7 – C8 – C14	112.3(1)

Atoms	Bond Angle (°)
C9 – C8 – C14	107.7(1)
C7 – C8 – H8	109.1(6)
C9 – C8 – H8	109.5(6)
C14 – C8 – H8	108.9(6)
C8 – C9 – C10	112.1(1)
C8 – C9 – C11	111.4(1)
C10 – C9 – C11	114.5(1)
C8 – C9 – H9	106.0(6)
C10 – C9 – H9	106.7(6)
C11 – C9 – H9	105.4(6)
C1 – C10 – C5	117.7(1)
C1 – C10 – C9	121.2(1)
C5 – C10 – C9	120.9(1)
C9 – C11 – C12	112.0(1)
C9 – C11 – H11A	111.2(6)
C9 – C11 – H11B	107.7(6)
C12 – C11 – H11A	108.2(6)
C12 – C11 – H11B	111.5(6)
H11A – C11 – H11B	106.0(8)
C11 – C12 – C13	111.5(1)
C11 – C12 – H12A	108.2(6)
C11 – C12 – H12B	108.6(6)
C13 – C12 – H12A	109.3(6)
C13 – C12 – H12B	110.7(6)
H12A – C12 – H12B	108.5(9)
C12 – C13 – C14	109.1(1)
C12 – C13 – C17	115.2(1)
C12 – C13 – C18	110.2(1)
C14 – C13 – C17	97.9(1)
C14 – C13 – C18	113.5(1)
C17 – C13 – C18	110.5(1)

Atoms	Bond Angle (°)
C8 – C14 – C13	113.4(1)
C8 – C14 – C15	120.3(1)
C13 – C14 – C15	103.9(1)
C8 – C14 – H14	105.8(6)
C13 – C14 – H14	105.6(6)
C15 – C14 – H14	106.8(6)
C14 – C15 – C16	103.6(1)
C14 – C15 – H15A	109.4(6)
C14 – C15 – H15B	107.5(6)
C16 – C15 – H15A	111.6(6)
C16 – C15 – H15B	112.9(6)
H15A – C15 – H15B	111.4(10)
C15 – C16 – C17	105.2(1)
C15 – C16 – H16A	112.9(6)
C15 – C16 – H16B	111.3(6)
C17 – C16 – H16A	110.1(6)
C17 – C16 – H16B	108.3(6)
H16A – C16 – H16B	109.0(9)
O2 – C17 – C13	117.1(1)
O2 – C17 – C16	114.7(1)
C13 – C17 – C16	104.4(1)
O2 – C17 – H17	104.1(6)
C13 – C17 – H17	107.2(6)
C16 – C17 – H17	109.0(6)
C13 – C18 – H18A	108.9(7)
C13 – C18 – H18B	111.6(6)
C13 – C18 – H18C	112.4(7)
H18A – C18 – H18B	109.0(9)
H18A – C18 – H18C	107.7(9)
H18B – C18 – H18C	107.1(10)

Table C-11. Bond angles for molecule 1 of 17β-estradiol•½methanol.

Atoms	Bond Angle (°)
C3' – O1' – H1O'	112.9(8)
C17' – O2' – H2O'	112.3(8)
C2' – C1' – C10'	122.2(1)
C2' – C1' – H1'	117.3(6)
C10' – C1' – H1'	120.4(6)
C1' – C2' – C3'	119.5(1)
C1' – C2' – H2'	122.4(6)
C3' – C2' – H2'	118.1(6)
O1' – C3' – C2'	118.4(1)
O1' – C3' – C4'	122.2(1)
C2' – C3' – C4'	119.4(1)
C3' – C4' – C5'	121.0(1)
C3' – C4' – H4'	118.9(6)
C5' – C4' – H4'	120.1(6)
C4' – C5' – C6'	117.7(1)
C4' – C5' – C10'	120.3(1)
C6' – C5' – C10'	122.0(1)
C5' – C6' – C7'	113.6(1)
C5' – C6' – H6C	107.7(6)
C5' – C6' – H6D	108.1(6)
C7' – C6' – H6C	111.4(6)
C7' – C6' – H6D	107.2(6)
H6C – C6' – H6D	108.7(9)
C6' – C7' – C8'	110.3(1)
C6' – C7' – H7C	110.3(6)
C6' – C7' – H7D	107.5(6)
C8' – C7' – H7C	108.9(6)
C8' – C7' – H7D	112.8(6)
H7C – C7' – H7D	107.1(8)
C7' – C8' – C9'	108.7(1)
C7' – C8' – C14'	112.9(1)
C9' – C8' – C14'	108.7(1)
C7' – C8' – H8'	106.6(6)

Atoms	Bond Angle (°)
C'9 – C8' – H8'	109.6(6)
C14' – C8' – H8'	110.3(6)
C8' – C9' – C10'	111.2(1)
C8' – C9' – C11'	111.9(1)
C10' – C9' – C11'	114.2(1)
C8' – C9' – H9'	105.1(6)
C10' – C9' – H9'	107.3(6)
C11' – C9' – H9'	106.4(6)
C1' – C10' – C5'	117.6(1)
C1' – C10' – C9'	121.4(1)
C5' – C10' – C9'	120.9(1)
C9' – C11' – C12'	112.2(1)
C9' – C11' – H11C	109.0(6)
C9' – C11' – H11D	108.1(6)
C12' – C11' – H11C	107.0(6)
C12' – C11' – H11D	109.7(6)
H11C – C11' – H11D	110.9(9)
C11' – C12' – C13'	111.1(1)
C11' – C12' – H12C	108.4(6)
C11' – C12' – H12D	108.9(6)
C13' – C12' – H12C	109.4(6)
C13' – C12' – H12D	111.8(6)
H12C – C12' – H12D	107.1(9)
C12' – C13' – C14'	108.4(1)
C12' – C13' – C17'	115.6(1)
C12' – C13' – C18'	110.1(1)
C14' – C13' – C17'	99.4(1)
C14' – C13' – C18'	113.5(1)
C17' – C13' – C18'	109.6(1)
C8' – C14' – C13'	113.3(1)
C8' – C14' – C15'	119.6(1)
C13' – C14' – C15'	103.7(1)
C8' – C14' – H14'	106.6(6)

Atoms	Bond Angle (°)
C13' – C14' – H14'	105.9(6)
C15' – C14' – H14'	106.8(6)
C14' – C15' – C16'	103.5(1)
C14' – C15' – H15C	110.5(6)
C14' – C15' – H15D	110.5(6)
C16' – C15' – H15C	112.2(6)
C16' – C15' – H15D	107.6(6)
H15C – C15' – H15D	112.1(9)
C15' – C16' – C17'	106.0(1)
C15' – C16' – H16C	112.1(6)
C15' – C16' – H16D	113.1(6)
C17' – C16' – H16C	110.0(6)
C17' – C16' – H16D	109.3(6)
H16C – C16' – H16D	106.4(10)
O2' – C17' – C13'	115.7(1)
O2' – C17' – C16'	112.8(1)
C13' – C17' – C16'	104.6(1)
O2' – C17' – H17'	103.2(6)
C13' – C17' – H17'	110.7(6)
C16' – C17' – H17'	109.9(6)
C13' – C18' – H18D	108.4(7)
C13' – C18' – H18E	112.6(7)
C13' – C18' – H18F	112.9(8)
H18D – C18' – H18E	107.1(9)
H18D – C18' – H18F	108.1(10)
H18E – C18' – H18F	107.6(10)
C19 – O3 – H3O	110.4(9)
O3 – C19 – H19A	110.0(5)
O3 – C19 – H19B	110.5(5)
O3 – C19 – H19C	111.3(5)
H19A – C19 – H19B	107.4(8)
H19A – C19 – H19C	111.3(8)
H19B – C19 – H19C	106.1(8)

Table C-12. Bond angles for molecule 2 and methanol of 17β-estradiol•½methanol.

Atom	Monopole Population ($P_{0,0}$)
O1	6.536(20)
O2	6.533(20)
C1	4.200(34)
C2	4.241(36)
C3	3.857(34)
C4	4.279(36)
C5	4.107(32)
C6	4.216(37)
C7	4.211(37)
C8	4.124(36)
C9	4.101(35)
C10	4.123(36)
C11	4.205(36)
C12	4.187(37)
C13	4.232(32)
C14	4.131(33)
C15	4.313(37)
C16	4.366(36)
C17	3.874(34)
C18	4.355(37)
O3	6.491(20)
C19	4.264(35)

Atom	Monopole Population ($P_{0,0}$)
O1'	6.539(21)
O2'	6.543(21)
C1'	4.194(36)
C2'	4.256(35)
C3'	3.875(34)
C4'	4.295(34)
C5'	4.123(34)
C6'	4.222(35)
C7'	4.199(34)
C8'	4.115(35)
C9'	4.115(33)
C10'	4.090(35)
C11'	4.215(36)
C12'	4.215(36)
C13'	4.220(34)
C14'	4.120(35)
C15'	4.309(37)
C16'	4.344(37)
C17'	3.852(33)
C18'	4.365(36)

Table C-13. Monopole populations (e^-) of non-H atoms of 17β-estradiol•½methanol.

Atom	Monopole Population ($P_{0,0}$)
H1O	0.665(19)
H2O	0.636(19)
H1	0.783(19)
H2	0.769(19)
H4	0.776(19)
H6A	0.826(14)
H6B	0.826(14)
H7A	0.842(14)
H7B	0.842(14)
H8	0.819(19)
H9	0.833(17)
H11A	0.833(14)
H11B	0.833(14)
H12A	0.837(14)
H12B	0.837(14)
H14	0.820(18)
H15A	0.857(15)
H15B	0.857(15)
H16A	0.872(14)
H16B	0.872(14)
H17	0.916(20)
H18A	0.887(13)
H18B	0.887(13)
H18C	0.887(13)
H3O	0.696(20)
H19A	0.850(12)
H19B	0.850(12)
H19C	0.850(12)

Atom	Monopole Population ($P_{0,0}$)
H1O'	0.638(18)
H2O'	0.651(18)
H1'	0.796(19)
H2'	0.788(21)
H4'	0.790(19)
H6C	0.832(15)
H6D	0.832(15)
H7C	0.842(14)
H7D	0.842(14)
H8'	0.803(18)
H9'	0.829(20)
H11C	0.827(15)
H11D	0.827(15)
H12C	0.841(14)
H12D	0.841(14)
H14'	0.821(19)
H15C	0.841(15)
H15D	0.841(15)
H16C	0.870(15)
H16D	0.870(15)
H17'	0.939(20)
H18D	0.879(13)
H18E	0.879(13)
H18F	0.879(13)

Table C-14. Monopole populations (e^-) of H atoms of 17β-estradiol•½methanol.

Multipoles	O1	O1'	O2	O2'	O3
$P_{1,+1}$	-0.025(17)	-0.033(17)	-0.043(17)	-0.028(18)	-0.046(20)
$P_{1,-1}$	0.030(19)	0.0	0.0	0.0	0.0
$P_{1,0}$	0.0	0.0	0.0	0.0	-0.068(19)
$P_{2,0}$	0.117(12)	0.127(13)	0.083(12)	0.089(12)	0.063(14)
$P_{2,+1}$	-0.033(11)	-0.016(12)	-0.021(11)	-0.018(11)	-0.038(14)
$P_{2,-1}$	-0.047(11)	-0.027(12)	0.0	-0.021(12)	-0.014(13)
$P_{2,+2}$	-0.042(11)	-0.035(11)	-0.077(11)	-0.046(11)	0.0
$P_{2,-2}$	-0.017(11)	0.0	0.0	0.0	0.0
$P_{3,0}$	-0.029(20)	0.0	0.0	0.050(22)	-0.040(25)
$P_{3,+1}$	-0.029(19)	0.0	0.0	0.0	-0.026(24)
$P_{3,-1}$	-0.028(20)	0.0	-0.024(20)	0.0	0.027(21)
$P_{3,+2}$	0.0	0.0	0.0	0.0	0.0
$P_{3,-2}$	0.0	0.034(21)	0.0	0.0	0.0
$P_{3,+3}$	0.083(18)	0.095(18)	0.075(19)	0.102(19)	0.073(20)
$P_{3,-3}$	-0.019(19)	0.0	0.0	-0.038(19)	-0.037(21)
$P_{4,0}$	0.037(19)	0.057(22)	0.0	0.025(20)	0.0
$P_{4,+1}$	0.0	-0.035(20)	0.0	0.0	0.0
$P_{4,-1}$	0.053(18)	0.0	0.025(18)	0.040(18)	0.0
$P_{4,+2}$	0.0	0.0	0.0	0.023(19)	0.023(22)
$P_{4,-2}$	0.0	0.0	0.0	0.021(19)	0.067(23)
$P_{4,+3}$	0.0	0.0	-0.039(18)	0.0	0.0
$P_{4,-3}$	0.0	-0.022(18)	0.020(18)	0.0	0.0
$P_{4,+4}$	0.024(16)	0.038(16)	0.0	0.0	0.020(18)
$P_{4,-4}$	0.0	0.036(17)	0.0	-0.020(16)	-0.030(20)

Table C-15. Multipole populations (e^-) of Oxygen atoms of 17β-estradiol•½methanol.

Multipoles	C1	C1'	C2	C2'	C3	C3'	C4	C4'	C5	C5'
$P_{1,+1}$	0.031(29)	0.051(29)	0.0	0.125(29)	0.0	0.082(23)	-0.056(28)	-0.036(28)	0.037(31)	0.0
$P_{1,-1}$	0.0	0.129(31)	-0.040(28)	0.0	0.080(22)	0.0	0.0	0.0	0.087(28)	-0.029(29)
$P_{1,0}$	0.0	0.032(29)	0.0	-0.049(29)	0.032(21)	-0.031(23)	0.0	0.0	0.0	-0.027(27)
$P_{2,0}$	-0.154(19)	-0.150(21)	-0.178(19)	-0.147(21)	-0.118(15)	-0.122(16)	-0.142(18)	-0.176(19)	-0.198(18)	-0.127(18)
$P_{2,+1}$	0.060(19)	0.045(20)	0.044(19)	0.0	-0.031(15)	-0.037(16)	-0.025(18)	0.0	-0.026(18)	0.065(18)
$P_{2,-1}$	0.029(19)	0.0	0.0	0.0	-0.018(15)	0.0	-0.068(18)	0.026(18)	0.027(18)	0.0
$P_{2,+2}$	0.039(18)	0.041(19)	0.0	0.064(19)	0.077(15)	0.039(16)	0.0	0.033(18)	0.033(18)	0.0
$P_{2,-2}$	0.019(18)	-0.054(19)	-0.041(19)	0.0	-0.048(15)	-0.024(15)	-0.058(18)	-0.028(19)	-0.048(19)	-0.035(18)
$P_{3,0}$	0.0	0.0	0.058(31)	0.0	-0.039(25)	0.0	0.0	0.0	0.0	0.0
$P_{3,+1}$	0.0	0.051(31)	0.0	0.0	0.045(24)	0.0	0.030(29)	0.0	0.0	0.0
$P_{3,-1}$	0.0	-0.042(31)	0.0	0.0	-0.036(23)	0.048(24)	-0.042(30)	0.047(30)	0.016(29)	0.052(29)
$P_{3,+2}$	0.0	0.0	0.0	0.0	0.032(24)	0.0	0.0	0.0	0.0	0.0
$P_{3,-2}$	0.0	0.0	0.0	0.0	0.0	0.0	0.0	-0.030(30)	0.0	0.0
$P_{3,+3}$	0.271(27)	0.298(27)	0.315(28)	0.318(28)	0.270(22)	0.222(22)	0.280(27)	0.294(27)	0.313(27)	0.288(29)
$P_{3,-3}$	0.0	0.082(31)	0.0	-0.006(30)	-0.029(26)	0.0	0.0	0.0	-0.068(31)	0.0

Multipoles	C6	C6'	C7	C7'	C8	C8'	C9	C9'	C10	C10'
$P_{1,+1}$	0.0	-0.071(26)	-0.033(25)	-0.091(27)	0.0	0.052(27)	0.0	0.0	0.066(29)	-0.062(29)
$P_{1,-1}$	0.038(25)	0.0	-0.043(25)	0.047(25)	-0.030(26)	0.0	0.056(27)	0.0	0.0	0.091(28)
$P_{1,0}$	-0.030(24)	-0.043(26)	-0.083(25)	-0.037(24)	-0.033(27)	0.035(26)	0.0	-0.055(27)	0.0	0.0
$P_{2,0}$	0.0	0.055(19)	0.022(18)	0.0	0.047(17)	-0.028(16)	0.034(17)	0.0	-0.213(19)	-0.133(19)
$P_{2,+1}$	-0.063(18)	0.0	0.0	0.020(17)	-0.047(17)	-0.017(16)	0.023(16)	0.017(17)	-0.021(18)	0.0
$P_{2,-1}$	0.0	-0.036(19)	0.0	0.0	-0.063(17)	-0.029(16)	0.049(17)	0.053(17)	0.048(18)	-0.020(19)
$P_{2,+2}$	0.055(17)	0.018(16)	0.025(17)	0.025(17)	0.0	-0.017(16)	-0.067(16)	-0.020(15)	0.0	0.0
$P_{2,-2}$	0.018(17)	0.0	-0.058(16)	0.0	0.0	0.076(17)	0.023(16)	0.072(17)	0.0	-0.023(18)
$P_{3,0}$	-0.048(30)	0.0	0.0	-0.035(28)	0.036(30)	0.057(29)	0.035(29)	0.0	0.0	-0.053(31)
$P_{3,+1}$	0.0	-0.088(28)	-0.071(28)	0.0	-0.053(28)	0.088(28)	0.067(26)	0.0	0.0	0.052(30)
$P_{3,-1}$	0.0	-0.060(28)	0.0	0.078(26)	0.0	0.080(26)	0.0	0.0	0.0	0.0
$P_{3,+2}$	-0.029(28)	0.0	0.073(29)	0.0	0.050(28)	-0.069(28)	-0.161(27)	-0.036(28)	0.0	0.0
$P_{3,-2}$	0.313(27)	0.241(29)	0.209(27)	0.256(28)	0.341(27)	0.295(28)	0.272(26)	-0.288(28)	-0.049(30)	0.0
$P_{3,+3}$	-0.113(27)	-0.165(25)	-0.151(25)	-0.153(28)	0.0	0.074(26)	0.053(26)	0.0	0.334(28)	0.295(27)
$P_{3,-3}$	-0.053(27)	0.0	0.080(27)	0.0	0.0	-0.037(27)	0.0	-0.032(26)	0.0	0.0

Table C-16. Multipole populations (e^-) of Carbon atoms of 17β-estradiol•½methanol.

Multipoles	C11	C11'	C12	C12'	C13	C13'	C14	C14'	C15	C15'
$P_{1,+1}$	-0.097(26)	0.0	-0.074(27)	0.0	-0.026(24)	0.0	0.0	0.0	0.0	-0.070(27)
$P_{1,-1}$	0.038(26)	0.0	0.0	0.049(25)	0.0	0.105(26)	0.032(25)	0.0	0.026(24)	0.076(26)
$P_{1,0}$	0.0	0.0	-0.039(23)	0.0	-0.027(26)	0.026(24)	-0.094(27)	0.0	0.034(24)	-0.053(25)
$P_{2,0}$	0.0	0.0	-0.044(18)	0.041(18)	0.026(18)	-0.031(17)	0.031(18)	0.020(17)	0.030(19)	-0.054(20)
$P_{2,+1}$	0.0	-0.045(18)	0.073(17)	0.067(17)	-0.052(17)	-0.095(17)	0.066(17)	-0.081(17)	0.0	-0.021(19)
$P_{2,-1}$	-0.095(17)	0.0	-0.034(17)	0.0	-0.024(17)	0.0	-0.023(17)	0.0	-0.071(18)	-0.059(19)
$P_{2,+2}$	0.0	0.047(17)	0.0	0.047(17)	0.0	0.0	0.0	0.0	0.070(18)	0.029(17)
$P_{2,-2}$	0.020(16)	-0.024(17)	-0.080(17)	-0.018(17)	0.0	0.058(17)	-0.025(16)	0.0	0.021(18)	-0.022(19)
$P_{3,0}$	-0.028(28)	0.036(30)	0.0	0.067(30)	0.044(30)	0.055(28)	-0.044(29)	0.064(26)	-0.039(30)	0.0
$P_{3,+1}$	-0.098(26)	-0.069(29)	-0.031(27)	-0.035(27)	-0.061(27)	0.085(27)	-0.094(28)	-0.042(28)	0.0	-0.048(29)
$P_{3,-1}$	0.0	-0.037(28)	0.044(27)	0.045(27)	0.0	0.099(26)	0.0	-0.113(27)	0.028(27)	0.0
$P_{3,+2}$	-0.042(28)	0.0	0.058(27)	0.0	0.096(28)	-0.036(28)	0.067(28)	0.0	-0.039(29)	0.0
$P_{3,-2}$	0.272(27)	0.295(28)	0.283(28)	0.267(27)	0.329(27)	0.332(27)	0.296(27)	0.307(27)	0.289(28)	0.236(30)
$P_{3,+3}$	-0.139(27)	-0.127(26)	-0.115(26)	-0.075(26)	-0.037(26)	0.034(26)	-0.099(25)	-0.077(28)	-0.115(28)	-0.181(28)
$P_{3,-3}$	0.0	0.049(27)	0.0	-0.033(26)	0.0	-0.077(28)	0.026(26)	0.060(27)	0.0	0.0

Multipoles	C16	C16'	C17	C17'	C18	C18'	C19
$P_{1,+1}$	0.0	-0.034(26)	0.028(20)	0.039(19)	-0.028(25)	-0.078(26)	-0.085(24)
$P_{1,-1}$	-0.031(25)	0.0	0.0	0.0	0.034(24)	0.097(24)	-0.028(26)
$P_{1,0}$	-0.061(26)	-0.049(24)	-0.067(18)	0.0	-0.034(24)	0.046(24)	0.025(25)
$P_{2,0}$	0.033(20)	0.0	-0.018(13)	0.028(14)	-0.017(17)	0.020(17)	0.080(21)
$P_{2,+1}$	0.0	-0.025(19)	0.052(13)	0.014(13)	-0.039(17)	0.0	0.0
$P_{2,-1}$	0.0	-0.050(20)	0.0	0.0	-0.016(16)	0.055(17)	0.020(19)
$P_{2,+2}$	0.0	0.0	0.0	0.0	0.054(18)	0.0	0.020(19)
$P_{2,-2}$	-0.019(18)	-0.030(18)	-0.078(13)	-0.031(13)	0.023(17)	0.059(18)	0.0
$P_{3,0}$	0.041(30)	0.059(30)	-0.074(22)	-0.066(21)	-0.028(29)	0.054(27)	0.177(32)
$P_{3,+1}$	-0.091(29)	0.0	-0.080(21)	-0.087(21)	0.0	0.110(28)	0.109(30)
$P_{3,-1}$	0.034(28)	0.022(29)	0.0	0.0	0.0	0.0	0.0
$P_{3,+2}$	0.0	-0.070(29)	0.074(22)	0.0	0.039(27)	0.072(28)	0.0
$P_{3,-2}$	0.274(28)	0.205(28)	0.212(21)	0.224(21)	0.212(26)	-0.229(28)	0.299(31)
$P_{3,+3}$	-0.135(25)	-0.116(28)	-0.076(21)	0.0	0.0	0.078(27)	0.091(30)
$P_{3,-3}$	0.061(26)	-0.039(27)	0.0	-0.021(20)	0.0	0.044(26)	0.0

Table C-17. Multipole populations (e^-) of Carbon atoms of 17β-estradiol•½methanol continued.

Atoms	$P_{1,0}$	$P_{2,0}$
H1O	0.121(19)	0.005(28)
H2O	0.125(21)	0.002(28)
H1	0.109(24)	-0.007(31)
H2	0.107(22)	0.066(32)
H4	0.127(23)	-0.018(30)
H6A	0.105(15)	-0.010(19)
H6B	0.105(15)	-0.010(19)
H7A	0.134(15)	0.034(20)
H7B	0.134(15)	0.034(20)
H8	0.150(23)	-0.029(31)
H9	0.089(22)	0.028(29)
H11A	0.110(16)	-0.015(21)
H11B	0.110(16)	-0.015(21)
H12A	0.099(16)	0.019(20)
H12B	0.099(16)	0.019(20)
H14	0.118(24)	-0.006(29)
H15A	0.070(17)	0.018(22)
H15B	0.070(17)	0.018(22)
H16A	0.132(16)	-0.005(22)
H16B	0.132(16)	-0.005(22)
H17	0.167(24)	0.041(33)
H18A	0.106(13)	-0.035(17)
H18B	0.106(13)	-0.035(17)
H18C	0.106(13)	-0.035(17)

Atoms	$P_{1,0}$	$P_{2,0}$
H1O'	0.127(19)	0.018(27)
H2O'	0.129(20)	0.012(28)
H1'	0.191(23)	0.006(29)
H2'	0.150(23)	0.043(34)
H4'	0.112(22)	0.049(28)
H6C	0.138(16)	0.024(22)
H6D	0.138(16)	0.024(22)
H7C	0.137(15)	0.051(21)
H7D	0.137(15)	0.051(21)
H8'	0.148(22)	0.056(30)
H9'	0.127(24)	0.065(32)
H11C	0.139(16)	0.033(22)
H11D	0.139(16)	0.033(22)
H12C	0.140(16)	-0.026(20)
H12D	0.140(16)	-0.026(20)
H14'	0.176(24)	0.058(31)
H15C	0.075(17)	0.062(23)
H15D	0.075(17)	0.062(23)
H16C	0.094(17)	-0.033(22)
H16D	0.094(17)	-0.033(22)
H17'	0.219(23)	0.062(35)
H18D	0.102(13)	0.012(17)
H18E	0.102(13)	0.012(17)
H18F	0.102(13)	0.012(17)
H3O	0.088(19)	-0.043(30)
H19A	0.183(13)	-0.036(19)
H19B	0.183(13)	-0.036(19)
H19C	0.183(13)	-0.036(19)

Table C-18. Multipole populations (e^-) of Hydrogen atoms of 17β-estradiol•½methanol.

Bond	$\rho(r_c)$	$\nabla^2\rho(r_c)$	R_{ij}	d_1	d_2	λ_1	λ_2	λ_3	ε
O1 – C3	1.992	-18.666	1.3731	0.8342	0.5389	-17.30	-13.85	12.49	0.25
O1' – C3'	2.101	-18.114	1.3692	0.8106	0.5586	-17.16	-15.42	14.46	0.11
O1 – H1O	2.379	-31.187	0.9702	0.7400	0.2302	-37.16	-36.51	42.48	0.02
O1' – H1O'	2.308	-28.991	0.9701	0.7502	0.2199	-37.32	-35.43	43.76	0.05
O2 – C17	1.734	-8.541	1.4259	0.8182	0.6078	-13.32	-11.42	16.21	0.17
O2' – C17'	1.863	-10.326	1.4294	0.8159	0.6136	-14.80	-13.62	18.10	0.09
O2 – H2O	2.303	-30.051	0.9704	0.7491	0.2213	-37.23	-35.63	42.80	0.05
O2' – H2O'	2.311	-26.715	0.9701	0.7415	0.2286	-35.18	-34.78	43.25	0.01
C1 – C2	2.160	-20.204	1.3930	0.7046	0.6884	-16.25	-12.87	8.92	0.26
C1' – C2'	2.111	-19.897	1.3934	0.7349	0.6585	-15.99	-12.24	8.32	0.31
C1 – C10	2.088	-18.453	1.4011	0.6823	0.7187	-15.30	-12.20	9.06	0.25
C1' – C10'	2.097	-19.229	1.4036	0.7295	0.6742	-15.82	-12.35	8.94	0.28
C1 – H1	1.807	-15.039	1.0804	0.6524	0.4280	-16.66	-14.94	16.55	0.12
C1' – H1'	1.785	-16.604	1.0800	0.6082	0.4718	-15.80	-13.51	12.70	0.17
C2 – C3	2.172	-21.192	1.3969	0.6614	0.7355	-16.77	-13.88	9.45	0.21
C2' – C3'	2.103	-18.329	1.3946	0.7454	0.6492	-16.33	-11.74	9.74	0.39
C2 – H2	1.884	-17.271	1.0801	0.6619	0.4182	-17.49	-16.52	16.74	0.06
C2' – H2'	1.891	-18.440	1.0800	0.6345	0.4456	-17.47	-15.48	14.50	0.13
C3 – C4	2.228	-21.634	1.3931	0.7152	0.6779	-17.78	-13.87	10.02	0.28
C3' – C4'	2.156	-19.354	1.3948	0.7118	0.6830	-16.37	-13.24	10.26	0.24
C4 – C5	2.095	-18.890	1.3993	0.6556	0.7437	-15.71	-11.94	8.76	0.32
C4' – C5'	2.078	-18.328	1.4012	0.6942	0.7070	-15.69	-11.90	9.27	0.32
C4 – H4	1.779	-12.634	1.0803	0.6507	0.4295	-15.43	-14.16	16.96	0.09
C4' – H4'	1.932	-18.229	1.0801	0.6569	0.4232	-17.81	-16.99	16.56	0.05
C5 – C6	1.705	-12.450	1.5112	0.7592	0.7520	-11.83	-10.57	9.95	0.12
C5' – C6'	1.694	-11.252	1.5127	0.7635	0.7492	-11.64	-9.88	10.26	0.18

Table C-19. Topological properties of bond critical points in 17β-estradiol•½methanol.

Bond	$\rho(r_c)$	$\nabla^2\rho(r_c)$	R_{ij}	d_1	D_2	λ_1	λ_2	λ_3	ε
C5 – C10	2.155	-20.813	1.4072	0.7180	0.6892	-16.33	-13.65	9.17	0.20
C5' – C10'	2.073	-18.203	1.4084	0.6742	0.7342	-15.25	-12.23	9.28	0.25
C6 – C7	1.583	-10.047	1.5249	0.7796	0.7453	-10.69	-9.50	10.14	0.13
C6' – C7'	1.626	-10.314	1.5248	0.7435	0.7813	-10.90	-9.62	10.20	0.13
C6 – H6A	1.691	-10.161	1.0900	0.6479	0.4421	-14.54	-12.47	16.85	0.17
C6 – H6B	1.776	-12.170	1.0923	0.6623	0.4300	-15.70	-14.71	18.24	0.07
C6' – H6C	1.881	-14.581	1.0906	0.6503	0.4403	-16.63	-14.99	17.04	0.11
C6' – H6D	1.872	-14.981	1.0901	0.6465	0.4436	-16.68	-14.86	16.57	0.12
C7 – C8	1.590	-9.180	1.5269	0.7957	0.7312	-10.18	-9.20	10.20	0.11
C7' – C8'	1.625	-9.958	1.5289	0.7494	0.7796	-10.77	-9.54	10.35	0.13
C7 – H7A	1.948	-16.835	1.0900	0.6574	0.4326	-18.12	-16.09	17.38	0.13
C7 – H7B	1.807	-14.807	1.0905	0.6387	0.4518	-15.99	-14.29	15.47	0.12
C7' – H7C	1.964	-17.201	1.0903	0.6551	0.4351	-18.26	-16.04	17.09	0.14
C7' – H7D	1.807	-14.724	1.0912	0.6361	0.4550	-15.79	-14.28	15.35	0.11
C8 – C9	1.581	-9.450	1.5438	0.7668	0.7770	-10.22	-9.47	10.24	0.08
C8' – C9'	1.545	-7.983	1.5457	0.7759	0.7697	-9.94	-8.59	10.54	0.16
C8 – C14	1.682	-11.473	1.5223	0.7540	0.7683	-11.40	-10.29	10.22	0.11
C8' – C14'	1.625	-10.656	1.5235	0.7202	0.8033	-11.05	-9.55	9.94	0.16
C8 – H8	1.813	-12.664	1.1003	0.6650	0.4353	-15.49	-15.16	17.98	0.02
C8' – H8'	1.923	-17.748	1.1009	0.6606	0.4404	-17.42	-16.56	16.23	0.05
C9 – C10	1.688	-11.912	1.5246	0.7404	0.7842	-11.75	-10.36	10.19	0.13
C9' – C10'	1.584	-9.752	1.5281	0.7594	0.7686	-10.43	-9.44	10.12	0.10
C9 – C11	1.489	-8.316	1.5378	0.7931	0.7447	-9.77	-8.35	9.80	0.17
C9' – C11'	1.585	-9.071	1.5412	0.7351	0.8060	-10.51	-9.12	10.56	0.15
C9 – H9	1.879	-15.456	1.1000	0.6783	0.4217	-17.66	-16.23	18.44	0.09
C9' – H9'	1.956	-17.951	1.1001	0.6668	0.4333	-18.16	-16.92	17.12	0.07

Table C-20. Topological properties of bond critical points in 17β-estradiol•½methanol continued.

Bond	$\rho(r_c)$	$\nabla^2\rho(r_c)$	R_{ij}	d_1	D_2	λ_1	λ_2	λ_3	ε
C11 – C12	1.589	-10.204	1.5382	0.7492	0.7890	-10.57	-9.72	10.09	0.09
C11' – C12'	1.541	-9.336	1.5408	0.7628	0.7779	-9.91	-9.41	9.98	0.05
C11 – H11A	1.789	-11.786	1.0901	0.6602	0.4299	-15.68	-14.41	18.30	0.09
C11 – H11B	1.813	-12.082	1.0900	0.6636	0.4264	-15.98	-14.81	18.71	0.08
C11' – H11C	1.810	-14.683	1.0924	0.6453	0.4472	-15.97	-14.68	15.96	0.09
C11' – H11D	1.845	-14.612	1.0902	0.6489	0.4413	-16.32	-14.86	16.57	0.10
C12 – C13	1.658	-11.077	1.5275	0.7506	0.7769	-11.03	-10.22	10.17	0.08
C12' – C13'	1.635	-9.576	1.5307	0.7501	0.7806	-11.01	-9.45	10.89	0.16
C12 – H12A	1.960	-16.160	1.0903	0.6768	0.4135	-18.65	-17.02	19.50	0.10
C12 – H12B	1.698	-12.630	1.0914	0.6421	0.4493	-14.77	-13.44	15.58	0.10
C12' – H12C	1.897	-14.894	1.0903	0.6570	0.4333	-17.33	-15.47	17.90	0.12
C12' – H12D	1.693	-10.342	1.0908	0.6354	0.4554	-14.31	-12.11	16.08	0.18
C13 – C14	1.538	-8.278	1.5423	0.7589	0.7834	-9.58	-8.85	10.15	0.08
C13' – C14'	1.643	-9.762	1.5434	0.7891	0.7543	-10.34	-9.90	10.48	0.04
C13 – C17	1.624	-8.277	1.5379	0.7470	0.7909	-10.54	-9.99	12.26	0.06
C13' – C17'	1.510	-6.686	1.5423	0.7449	0.7974	-9.53	-8.74	11.58	0.09
C13 – C18	1.668	-9.648	1.5368	0.7767	0.7602	-10.68	-10.13	11.16	0.05
C13' – C18'	1.715	-10.914	1.5332	0.7625	0.7707	-11.10	-10.93	11.11	0.01
C14 – C15	1.580	-9.879	1.5414	0.7578	0.7836	-10.46	-9.46	10.04	0.11
C14' – C15'	1.586	-9.229	1.5363	0.7506	0.7858	-10.41	-9.10	10.28	0.14
C14 – H14	1.910	-15.081	1.1001	0.6761	0.4240	-17.45	-16.21	18.58	0.08
C14' – H14'	2.006	-20.475	1.1000	0.6528	0.4472	-18.50	-17.49	15.51	0.06
C15 – C16	1.525	-8.303	1.5532	0.7550	0.7982	-10.05	-8.63	10.38	0.17
C15' – C16'	1.492	-7.757	1.5508	0.8012	0.7496	-9.89	-8.13	10.26	0.22
C15 – H15A	1.763	-11.798	1.0901	0.6645	0.4256	-16.19	-14.26	18.65	0.14
C15 – H15B	1.777	-10.781	1.0909	0.6711	0.4198	-15.74	-14.73	19.69	0.07

Table C-21. Topological properties of bond critical points in 17β-estradiol•½methanol continued.

Bond	$\rho(r_c)$	$\nabla^2\rho(r_c)$	R_{ij}	d_1	D_2	λ_1	λ_2	λ_3	ε
C15' – H15C	1.882	-15.052	1.0903	0.6688	0.4216	-18.03	-15.33	18.32	0.18
C15' – H15D	1.751	-13.044	1.0913	0.6552	0.4361	-15.90	-14.21	17.07	0.12
C16 – C17	1.638	-9.824	1.5461	0.7828	0.7633	-11.30	-10.29	11.77	0.10
C16' – C17'	1.542	-7.493	1.5512	0.7795	0.7717	-9.98	-9.31	11.80	0.07
C16 – H16A	1.906	-15.286	1.0901	0.6486	0.4414	-16.96	-15.61	17.28	0.09
C16 – H16B	1.797	-13.408	1.0905	0.6364	0.4541	-14.93	-14.58	16.11	0.02
C16' – H16C	1.703	-8.472	1.0901	0.6520	0.4381	-14.36	-12.68	18.56	0.13
C16' – H16D	1.678	-8.319	1.0901	0.6487	0.4414	-13.95	-12.55	18.18	0.11
C17 – H17	2.018	-17.771	1.1000	0.6630	0.4371	-19.36	-18.82	20.41	0.03
C17' – H17'	2.067	-20.809	1.1006	0.6409	0.4597	-20.06	-18.79	18.05	0.07
C18 – H18A	1.812	-11.307	1.0600	0.6184	0.4416	-14.71	-13.64	17.05	0.08
C18 – H18B	1.844	-14.261	1.0605	0.6164	0.4441	-15.77	-14.74	16.25	0.07
C18 – H18C	1.850	-13.230	1.0603	0.6200	0.4403	-15.57	-14.56	16.90	0.07
C18' – H18D	1.762	-12.273	1.0691	0.6267	0.4424	-15.13	-14.29	17.15	0.06
C18' – H18E	1.910	-16.290	1.0611	0.6251	0.4360	-17.09	-15.73	16.53	0.09
C18' – H18F	1.933	-14.147	1.0610	0.6344	0.4265	-17.57	-14.76	18.18	0.19
O3 – C19	1.964	-12.936	1.4239	0.8367	0.5872	-14.50	-13.07	14.64	0.11
O3 – H3O	2.346	-19.388	0.9417	0.7160	0.2257	-35.13	-33.93	49.67	0.04
C19 – H19A	1.785	-12.350	1.0820	0.6237	0.4583	-15.47	-13.65	16.77	0.13
C19 – H19B	1.970	-19.275	1.0731	0.6177	0.4554	-18.20	-15.96	14.88	0.14
C19 – H19C	1.911	-14.353	1.0702	0.6159	0.4543	-17.14	-12.99	15.78	0.32

Table C-22. Topological properties of bond critical points in 17β-estradiol•½methanol continued.

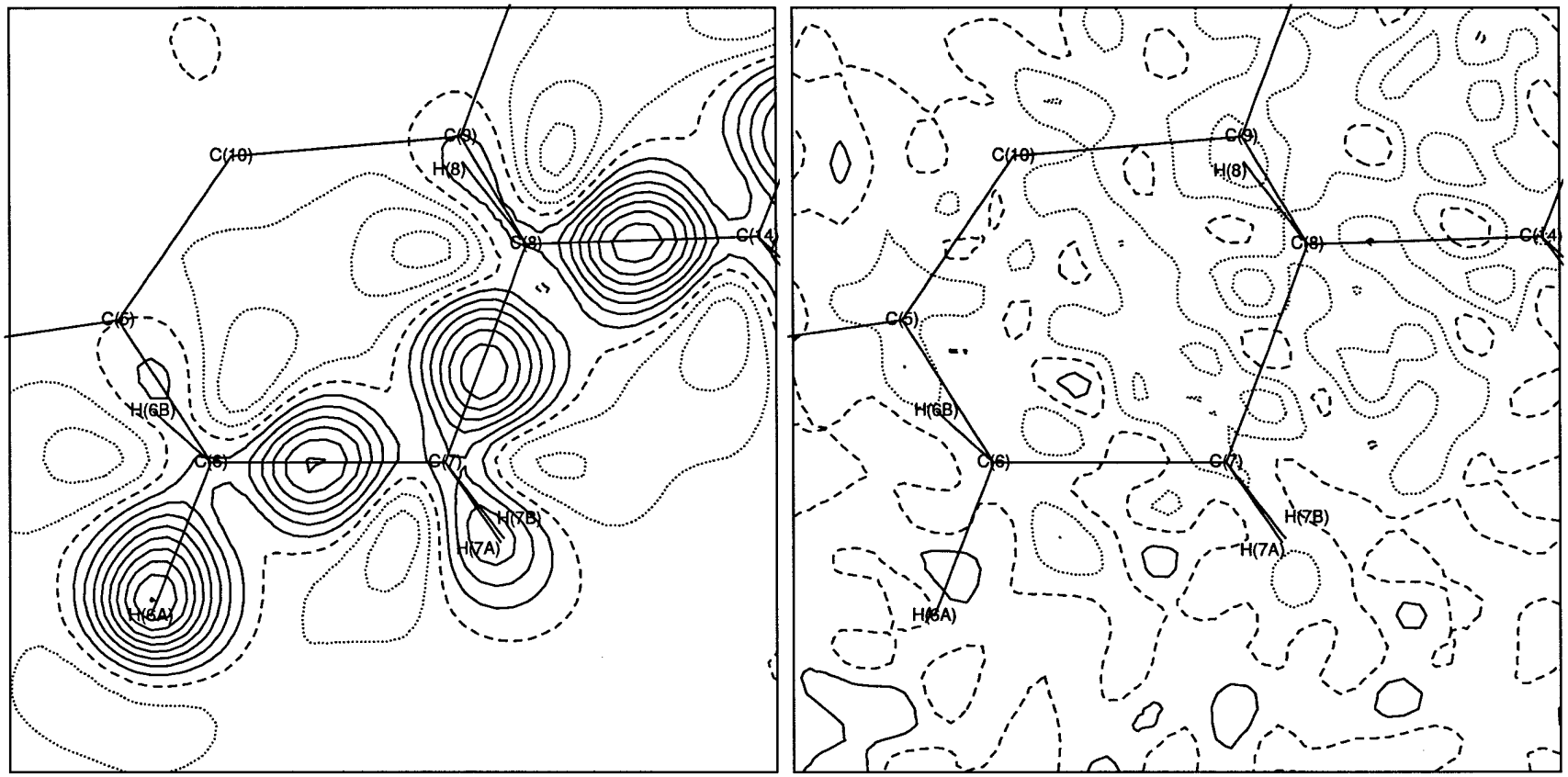

Figure C-3. Dynamic model map and residual map in the C6 – C7 – C8 plane of 17β-estradiol•½methanol. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

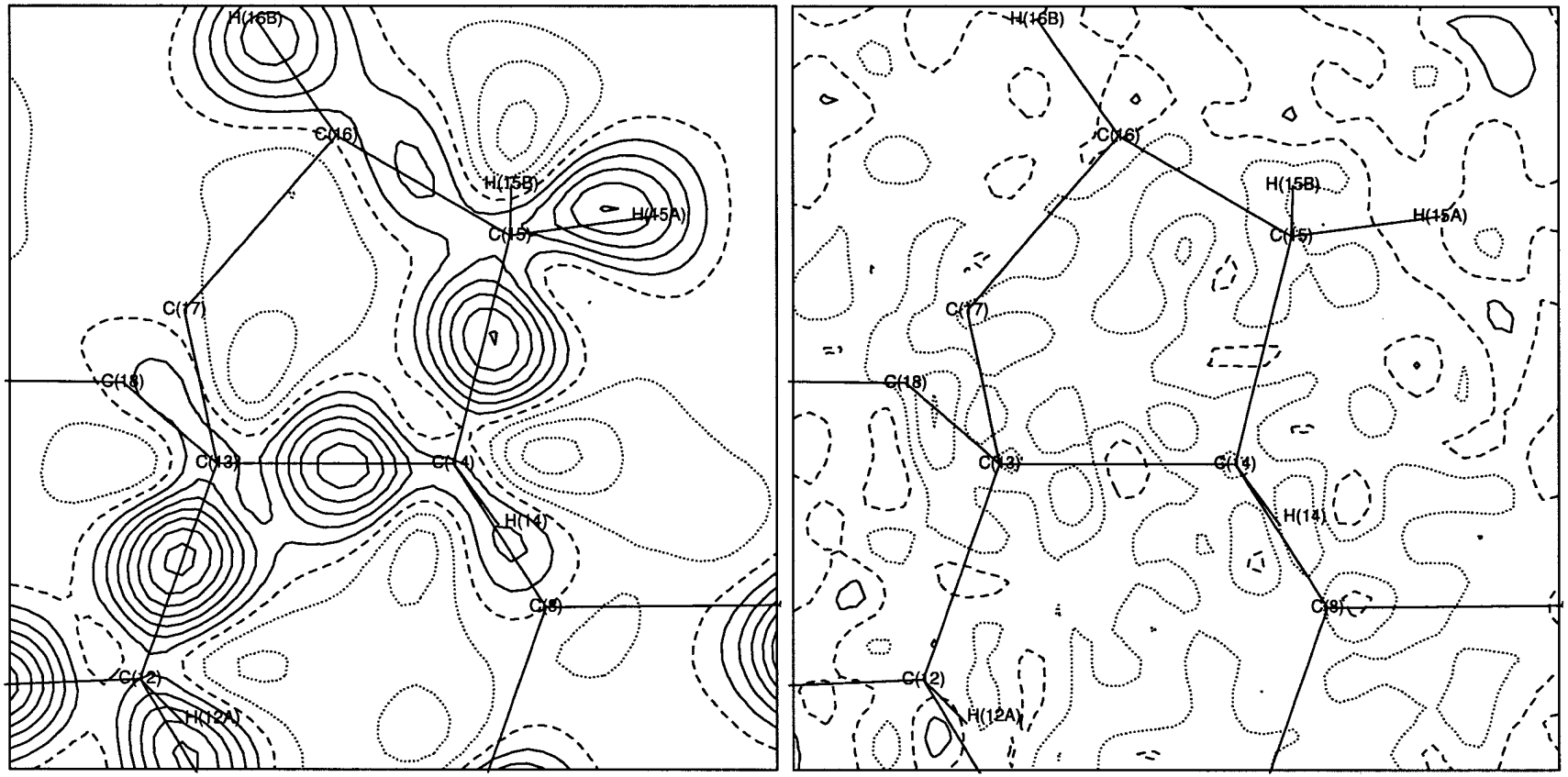

Figure C-4. Dynamic model map and residual map in the C13 – C14 – C15 plane of 17β-estradiol•½methanol. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

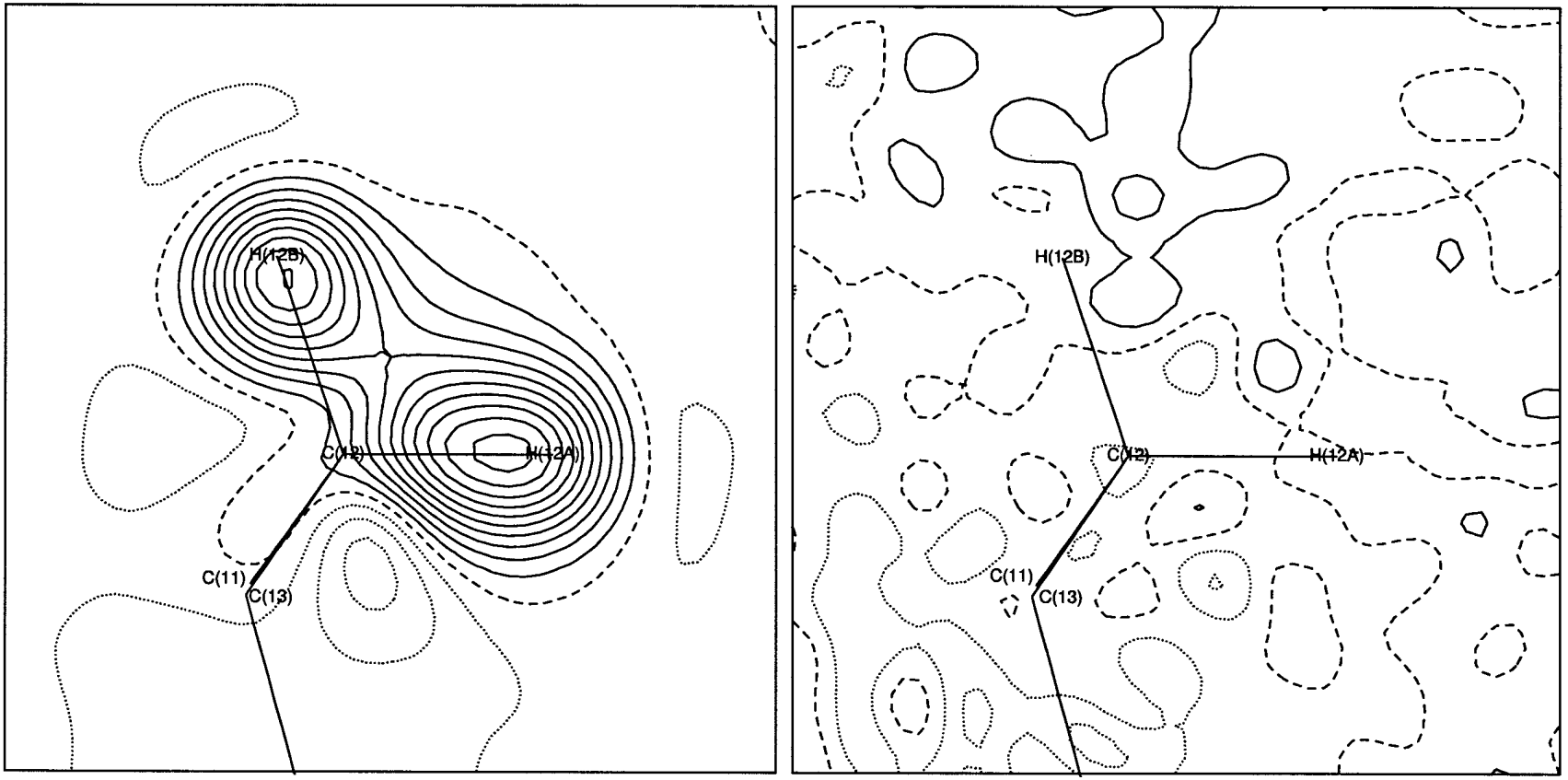

Figure C-5. Dynamic model map and residual map in the C12 – H12A – H12B plane of 17β-estradiol•½methanol. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

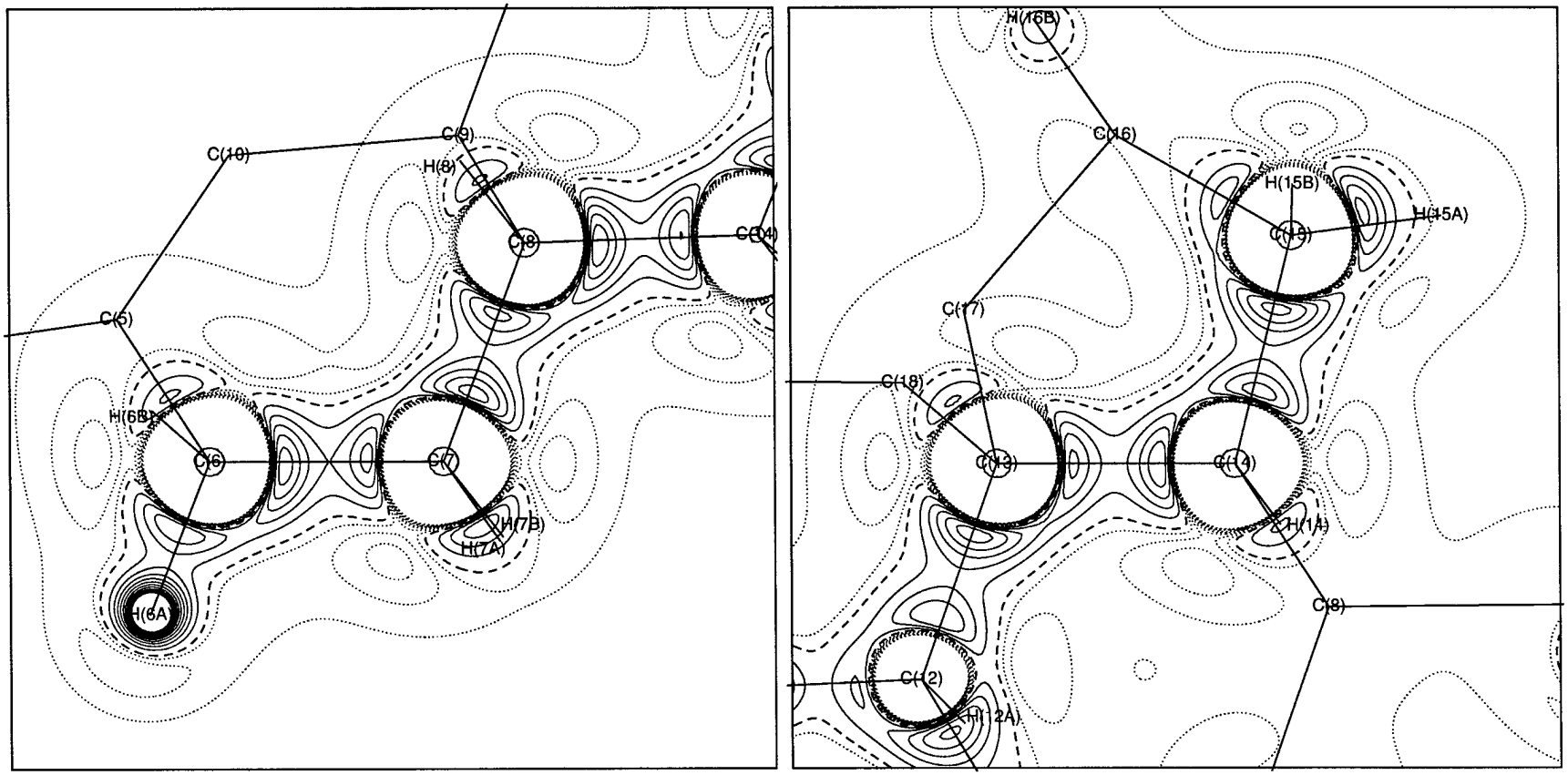

Figure C-6. The Laplacian of the total electron density of atoms at rest in the C6 – C7 – C8 and C13 – C14 – C15 planes of 17β-estradiol•½methanol. Contour intervals are 5 eÅ^{-5} starting at 5 eÅ^{-5} (solid blue lines), -2 eÅ^{-5} starting at -2 eÅ^{-5} (dotted red lines), and the dashed line equals 0 eÅ^{-5}.

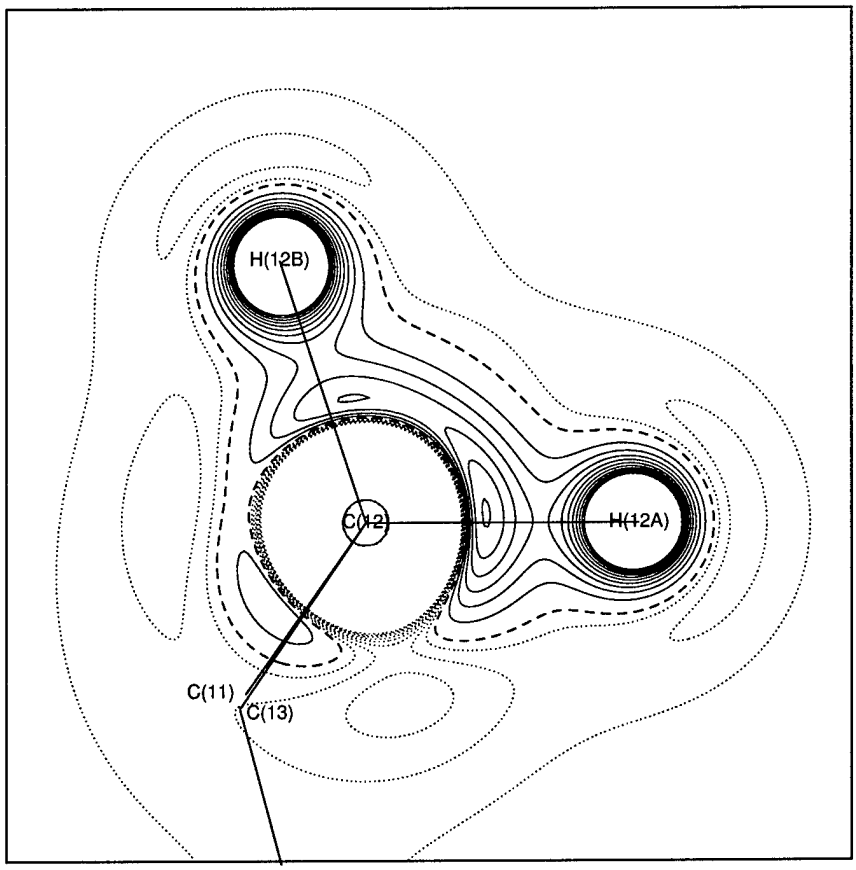

Figure C-7. The Laplacian of the total electron density of atoms at rest in the H12A – C12 – H12B plane of 17β-estradiol•½methanol. Contour intervals are 5 eÅ^{-5} starting at 5 eÅ^{-5} (solid blue lines), -2 eÅ^{-5} starting at -2 eÅ^{-5} (dotted red lines), and the dashed line plots 0 eÅ^{-5}.

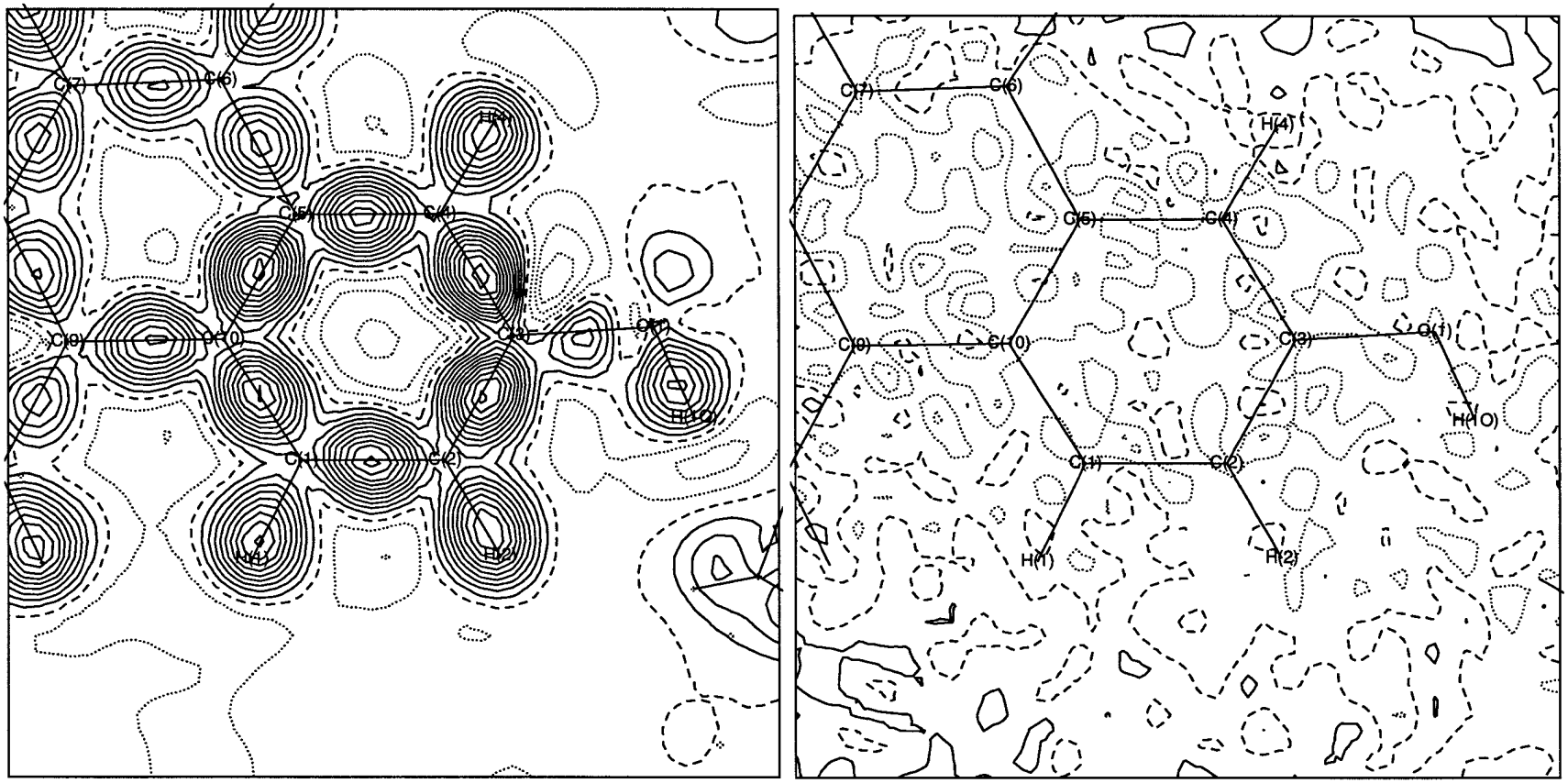

Figure C-8. Dynamic model map and residual map in the plane of the aromatic ring of molecule 1 of 17β-estradiol•½methanol. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

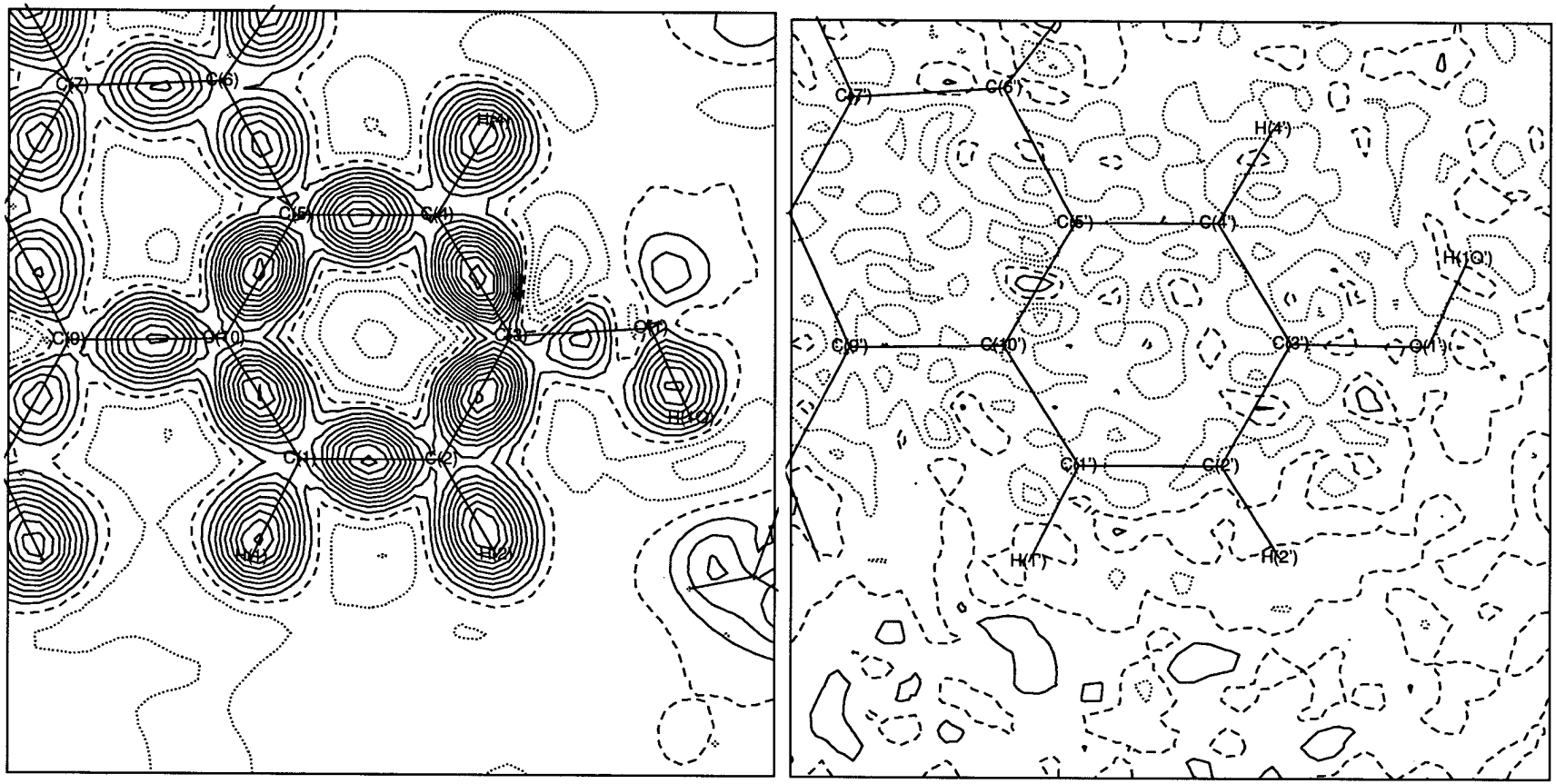

Figure C-9. Dynamic model map and residual map in the plane of the aromatic ring of molecule 2 of 17β-estradiol•½methanol. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

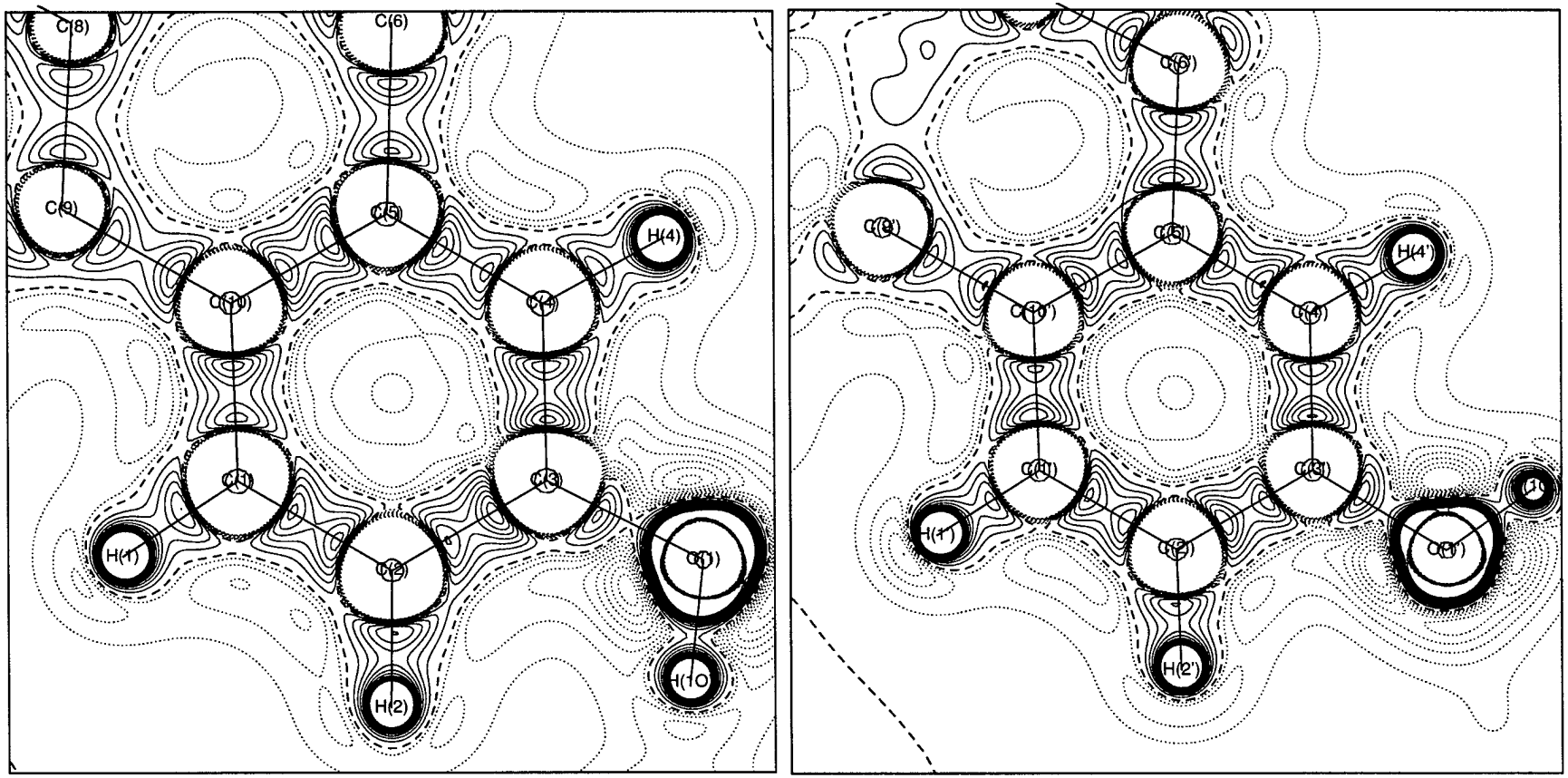

Figure C-10. The Laplacian of the total electron density of atoms at rest in the plane of the aromatic rings of 17β-estradiol•½methanol. Contour intervals are 5 eÅ^{-5} starting at 5 eÅ^{-5} (solid blue lines), -2 eÅ^{-5} starting at -2 eÅ^{-5} (dotted red lines), and the dashed line plots 0 eÅ^{-5}.

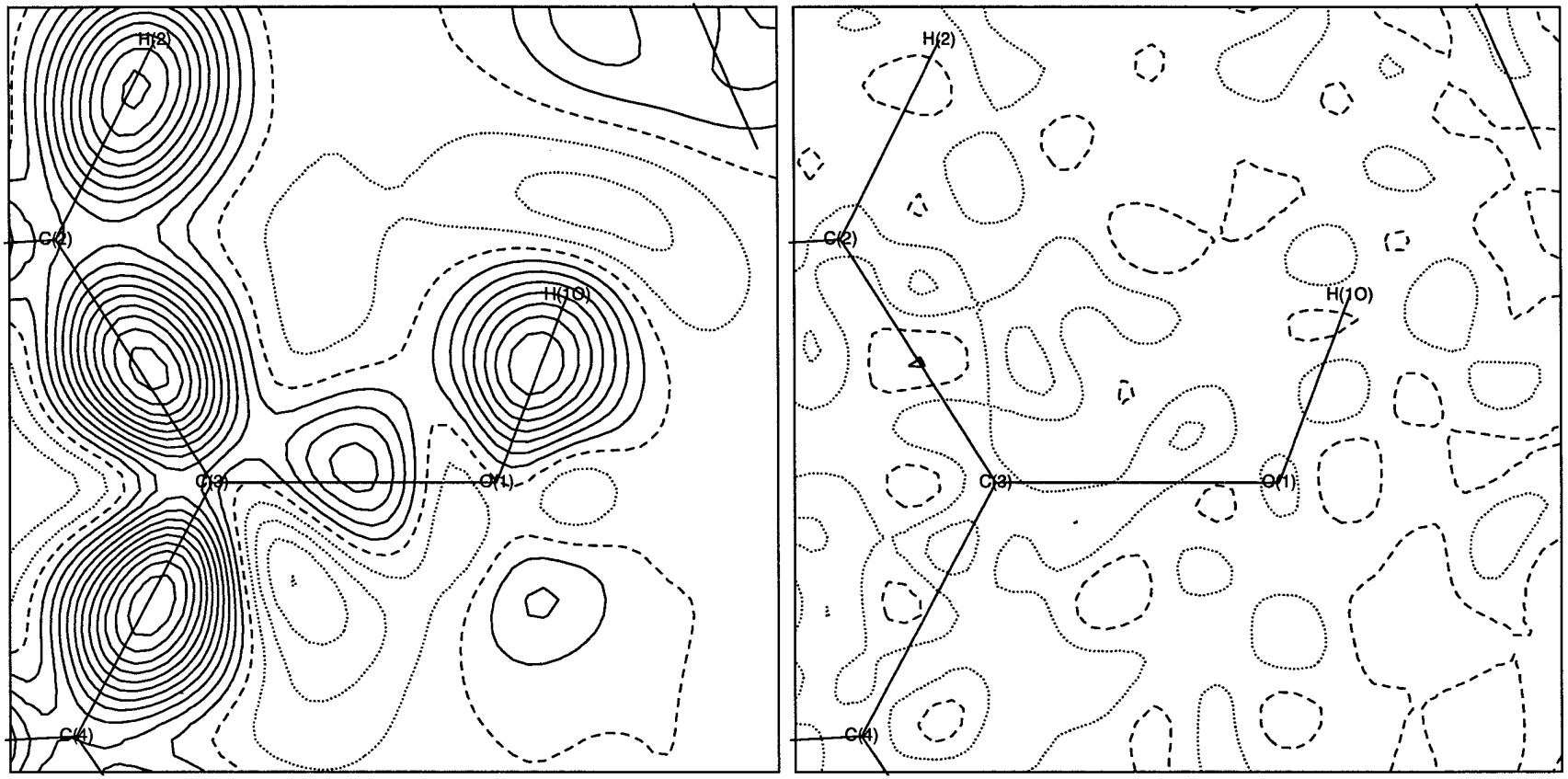

Figure C-11. Dynamic model map and residual map in the C3 – O1 – H1O plane of 17β-estradiol•½methanol. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

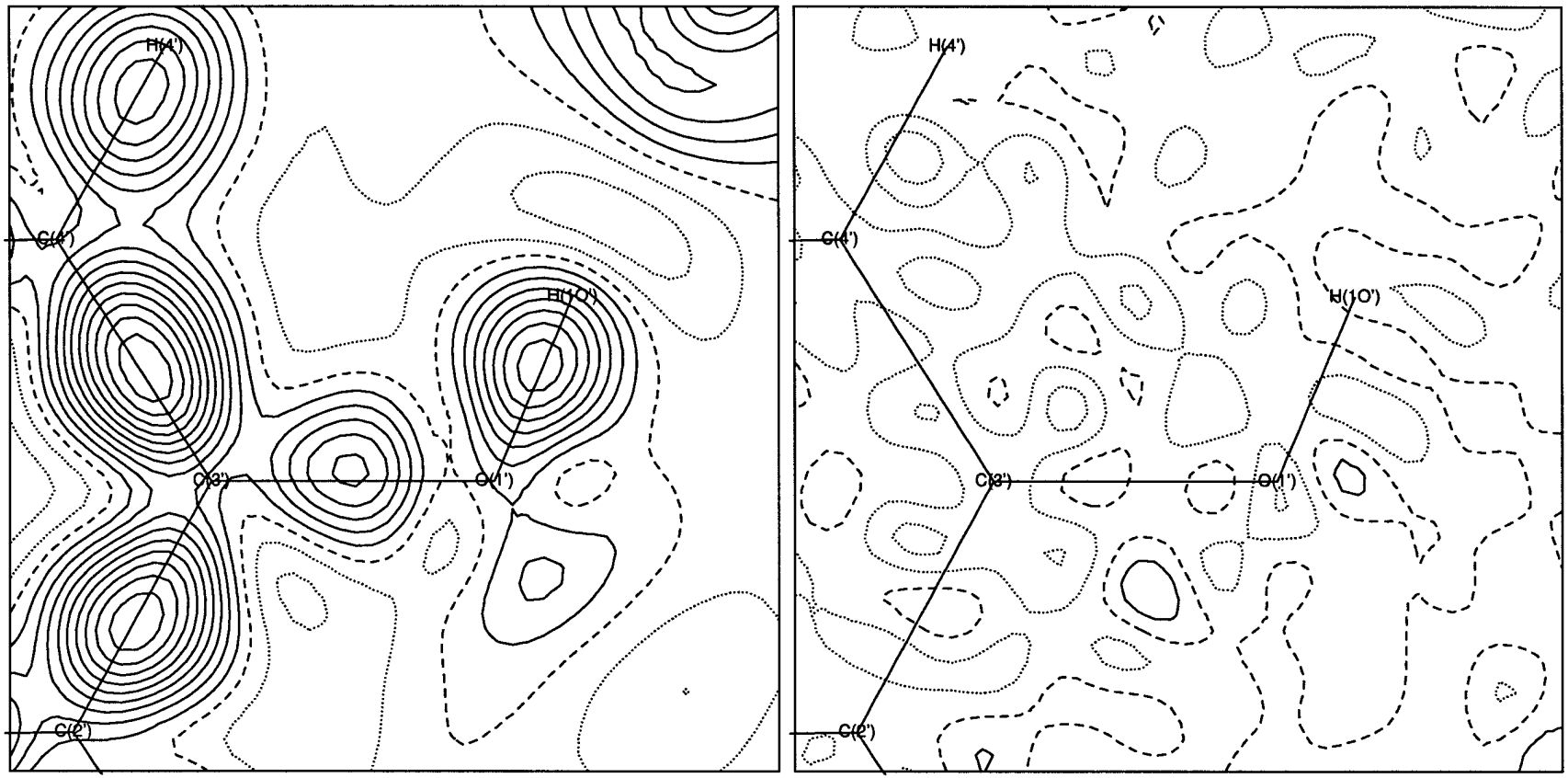

Figure C-12. Dynamic model map and residual map in the C3' – O1' – H1O' plane of 17β-estradiol•½methanol. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

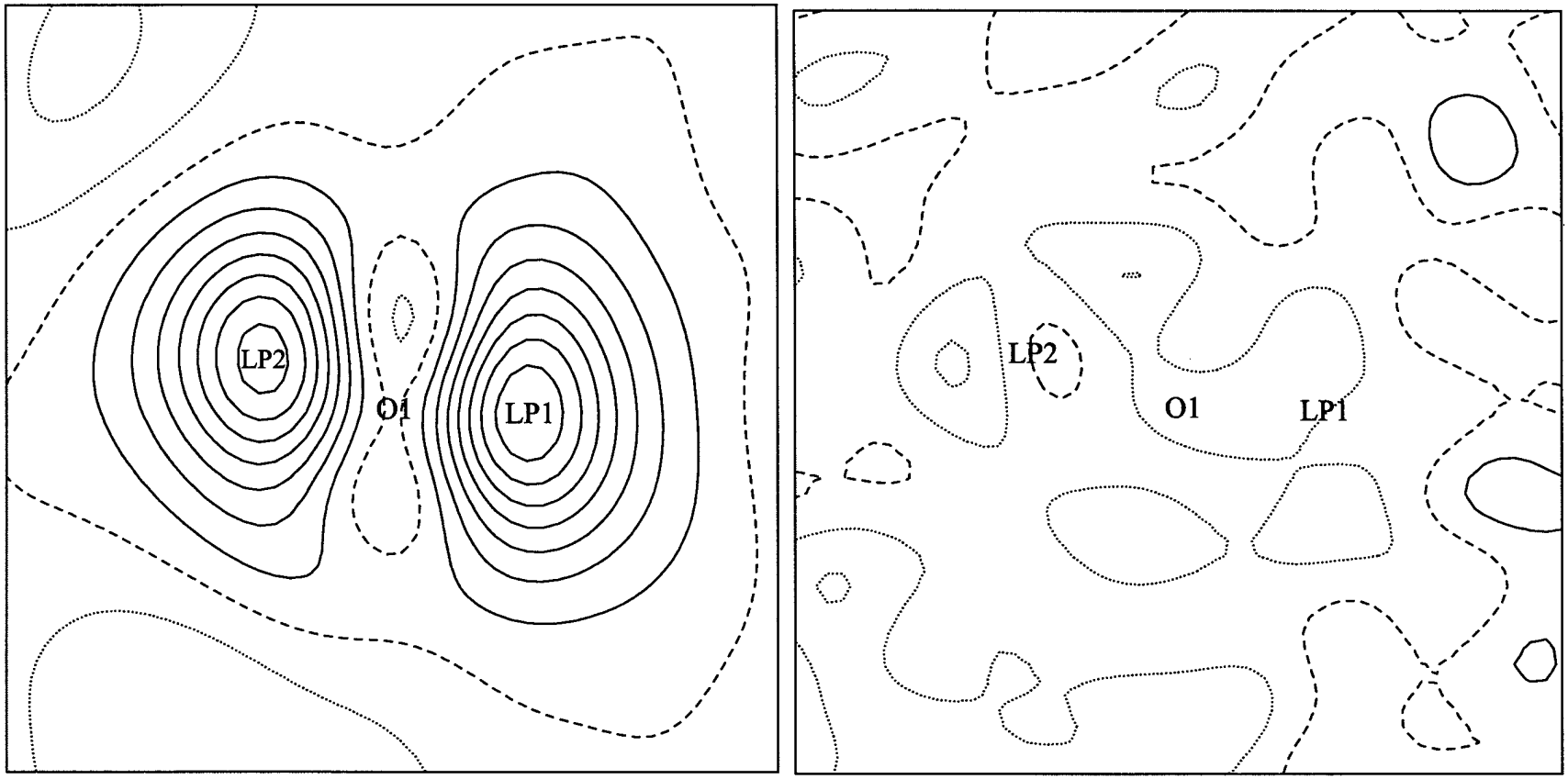

Figure C-13. Dynamic model map and residual map in the plane of the lone pairs of O1 of 17β-estradiol•½methanol. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

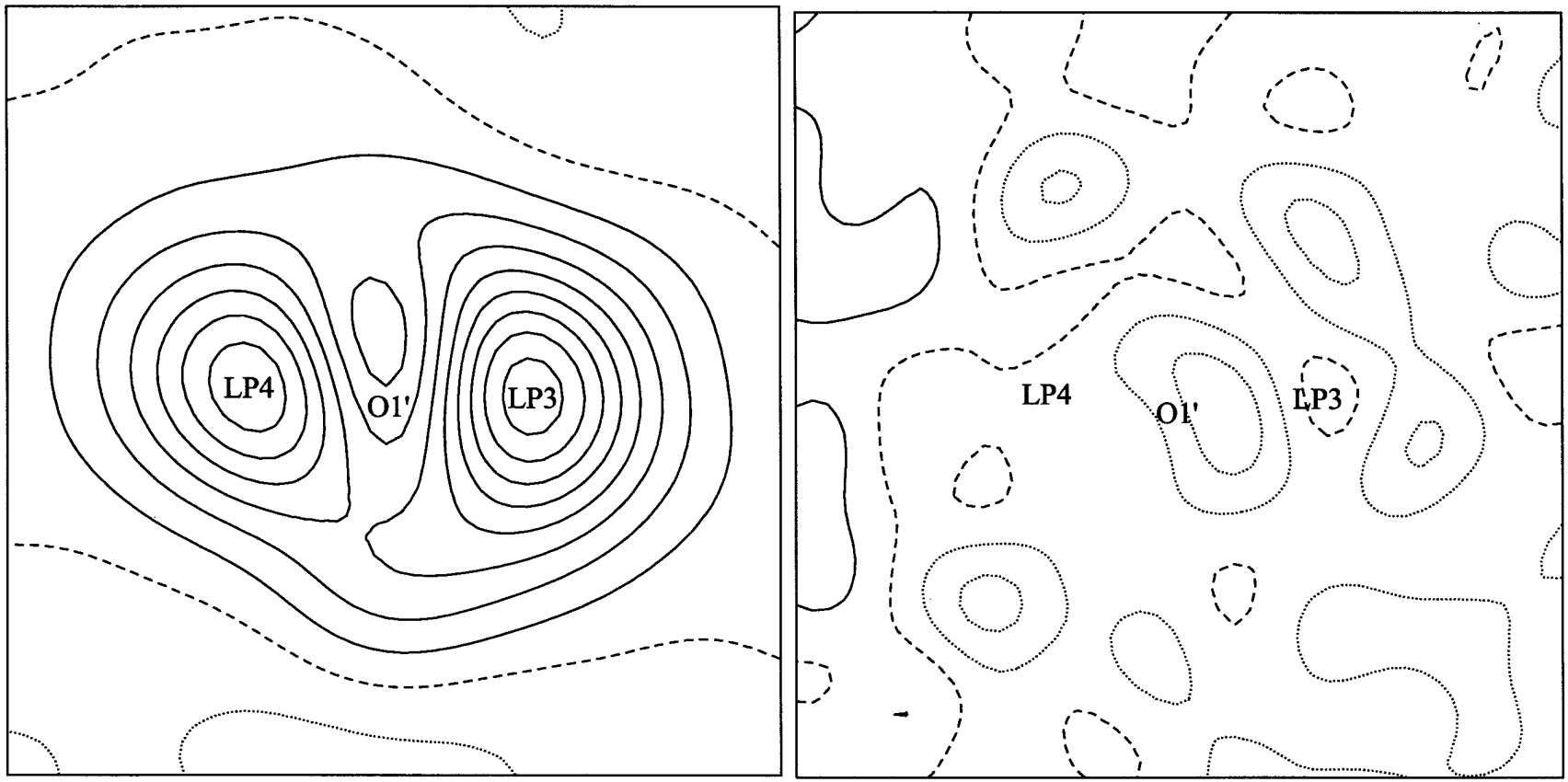

Figure C-14. Dynamic model map and residual map in the plane of the lone pairs of O1' of 17β-estradiol•½methanol. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

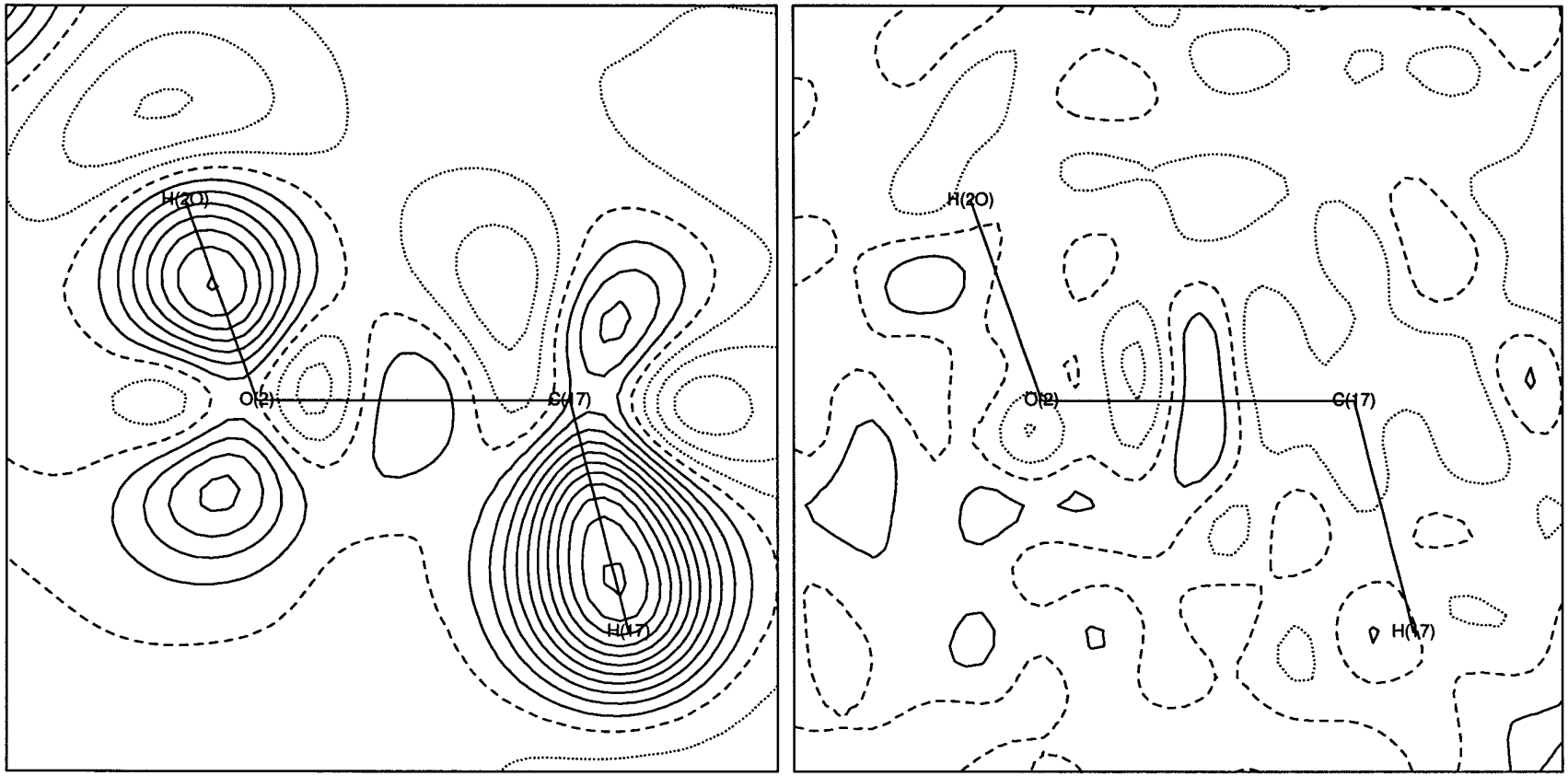

Figure C-15. Dynamic model map and residual map in the C17 – O2 – H2O plane of 17β-estradiol•½methanol. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

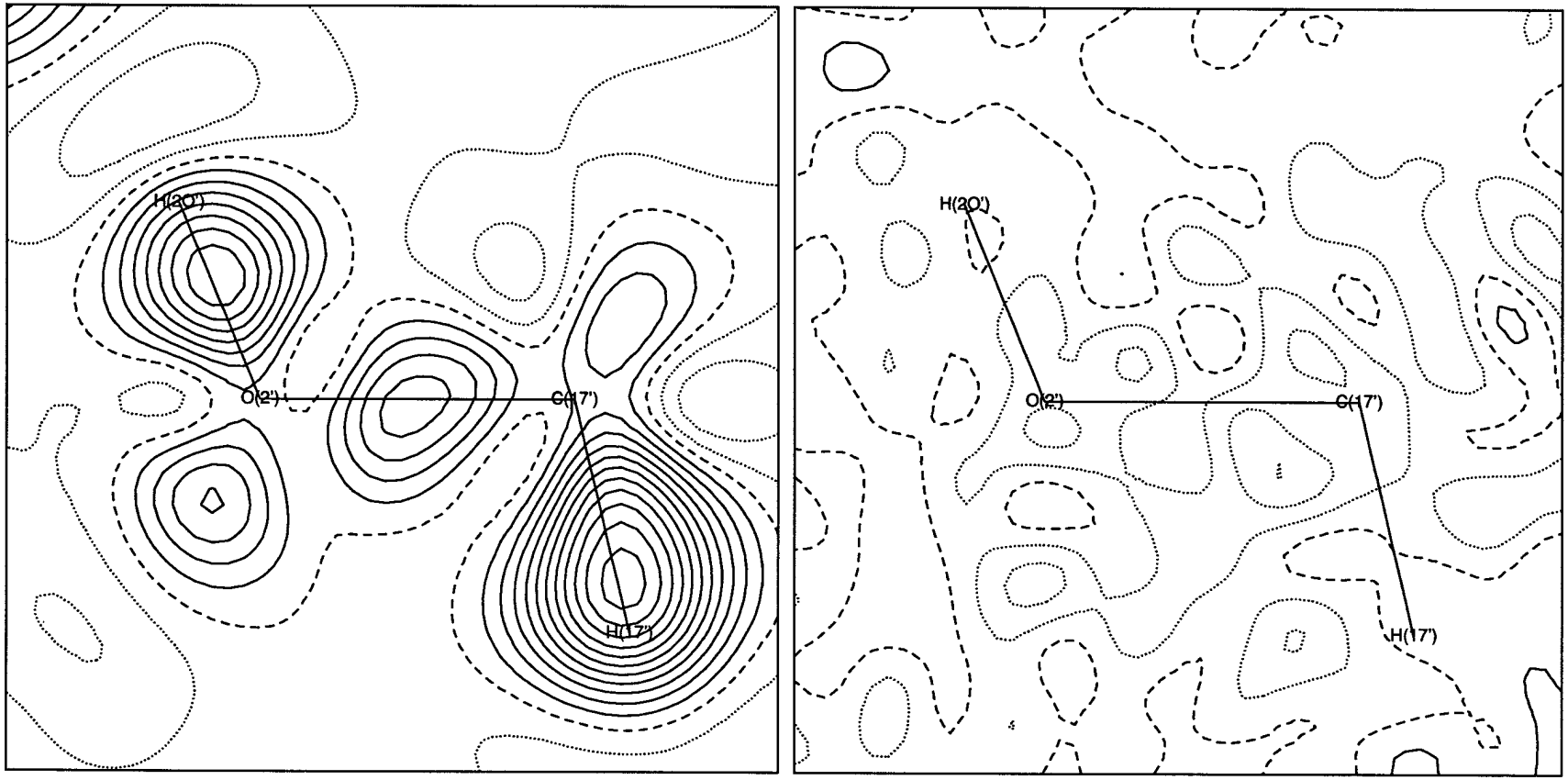

Figure C-16. Dynamic model map and residual map in the C17' – O2' – H2O' plane of 17β-estradiol•½methanol. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

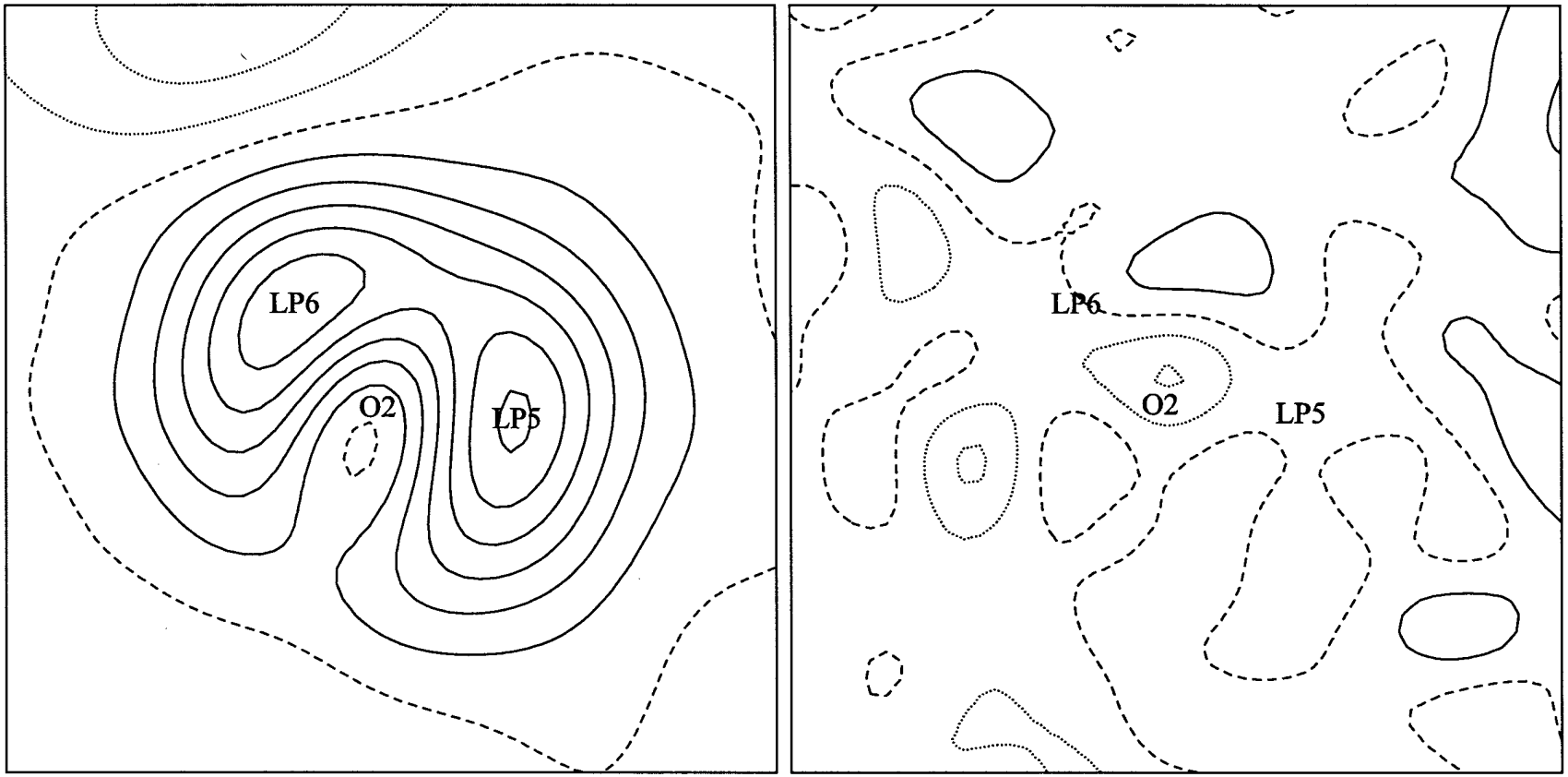

Figure C-17. Dynamic model map and residual map in the plane of the lone pairs of O2 of 17β-estradiol•½methanol. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

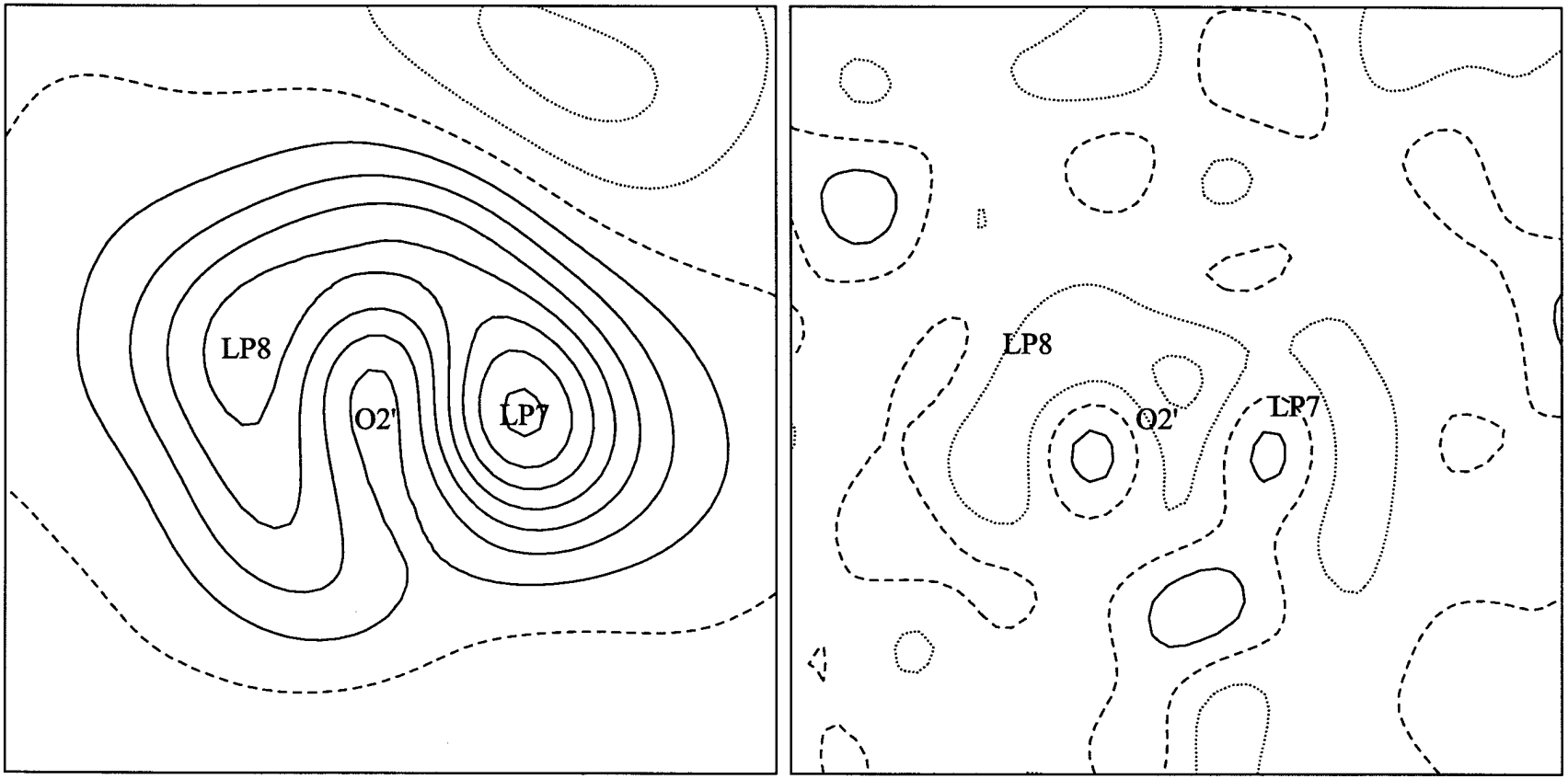

Figure C-18. Dynamic model map and residual map in the plane of the lone pairs of O2' of 17β-estradiol•½methanol. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

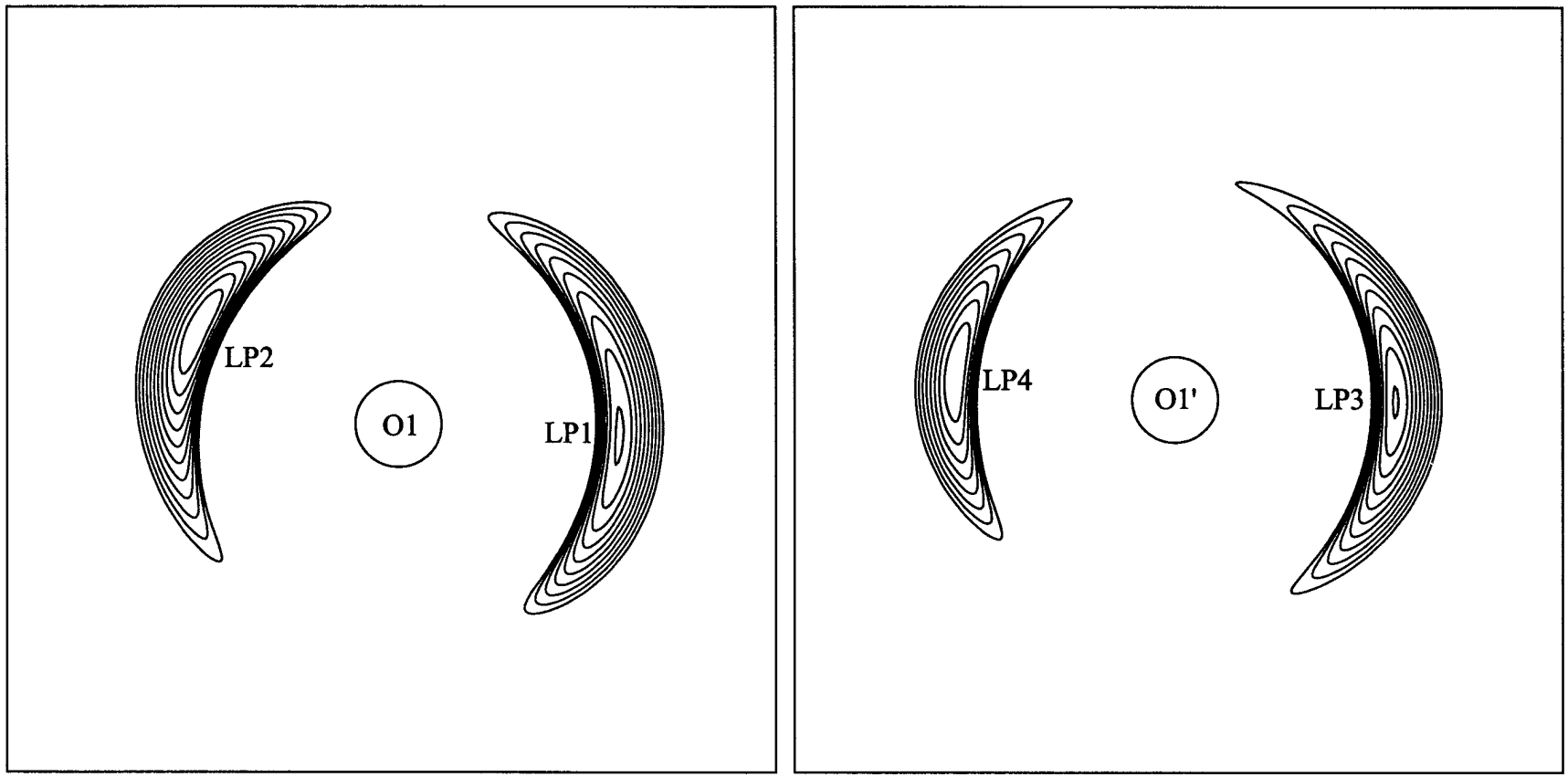

Figure C-19. The Laplacian of the total electron density of atoms at rest in the plane of the lone pairs of the O1 and O1' of 17β-estradiol•½methanol. Contour intervals are 5 eÅ^{-5} starting at 80 eÅ^{-5}.

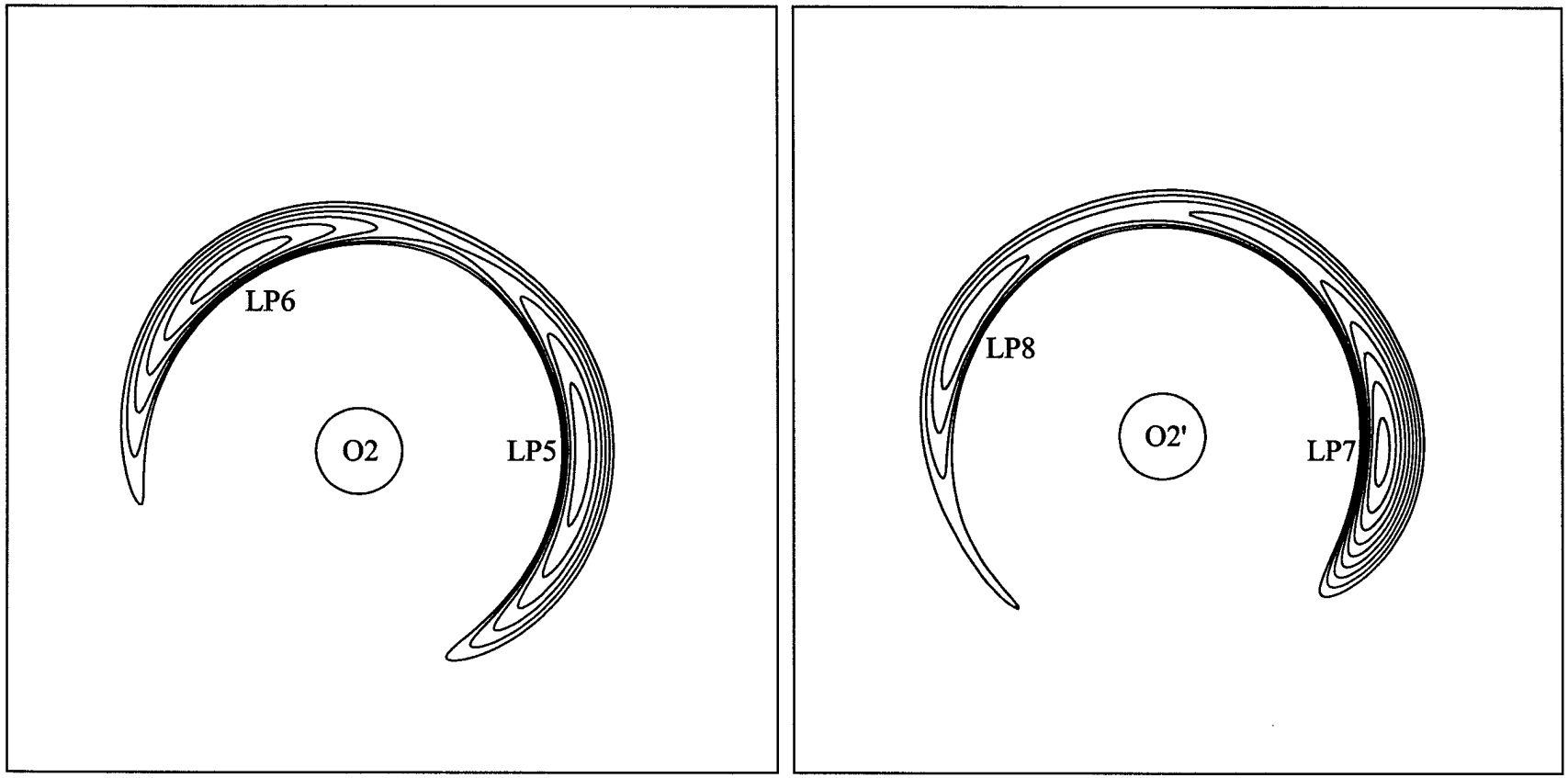

Figure C-20. The Laplacian of the total electron density of atoms at rest in the plane of the lone pairs of the O2 and O2' of 17β-estradiol•½methanol. Contour intervals are 5 eÅ^{-5} starting at 90 eÅ^{-5}.

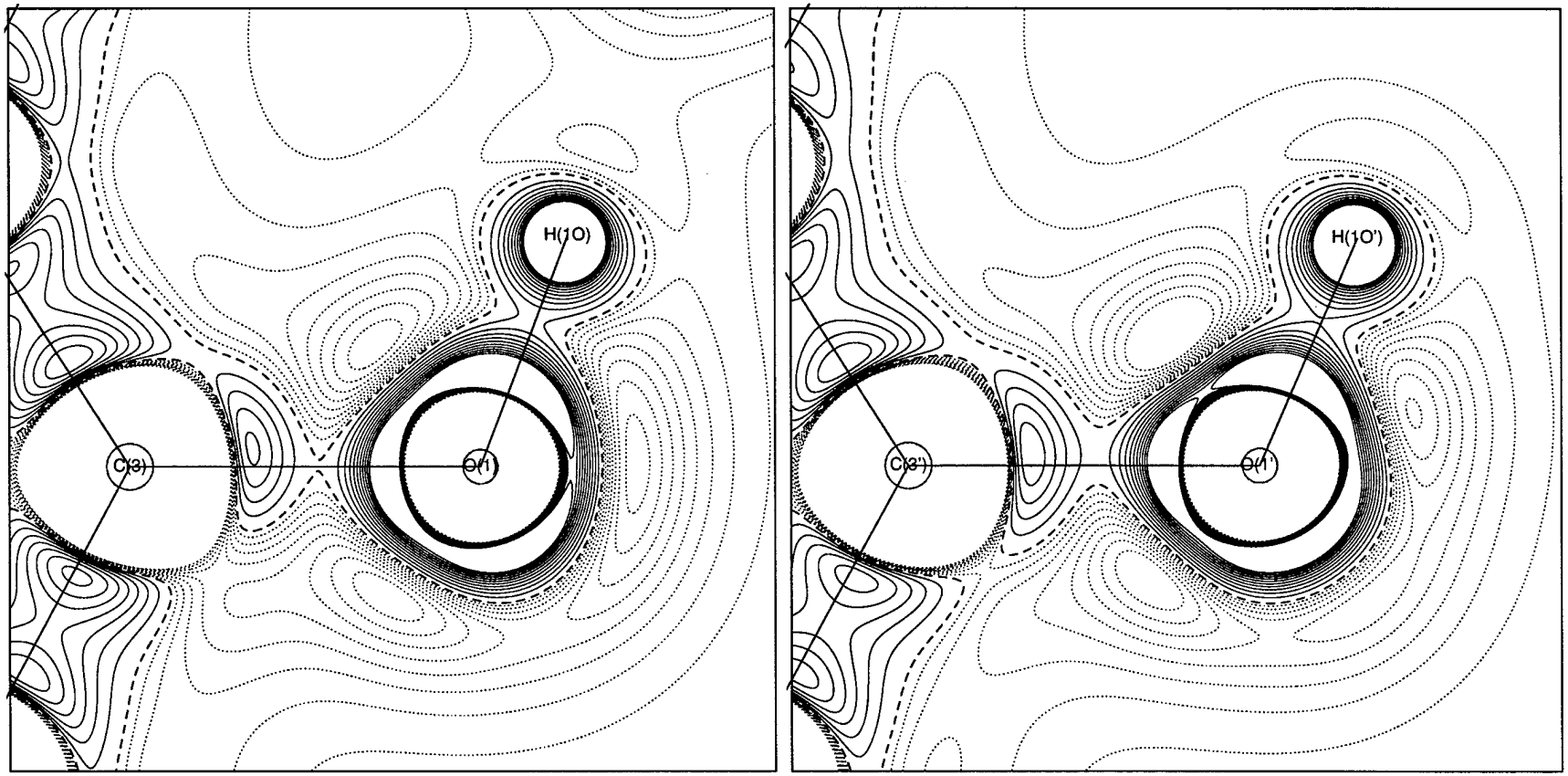

Figure C-21. The Laplacian of the total electron density of atoms at rest in the C3–O1–H1O plane and C3'–O1'–H1O' of 17β-estradiol•½methanol. Contour intervals are 5 eÅ^{-5} starting at 5 eÅ^{-5} (solid blue lines), -2 eÅ^{-5} starting at -2 eÅ^{-5} (dotted red lines), and the dashed line plots 0 eÅ^{-5}.

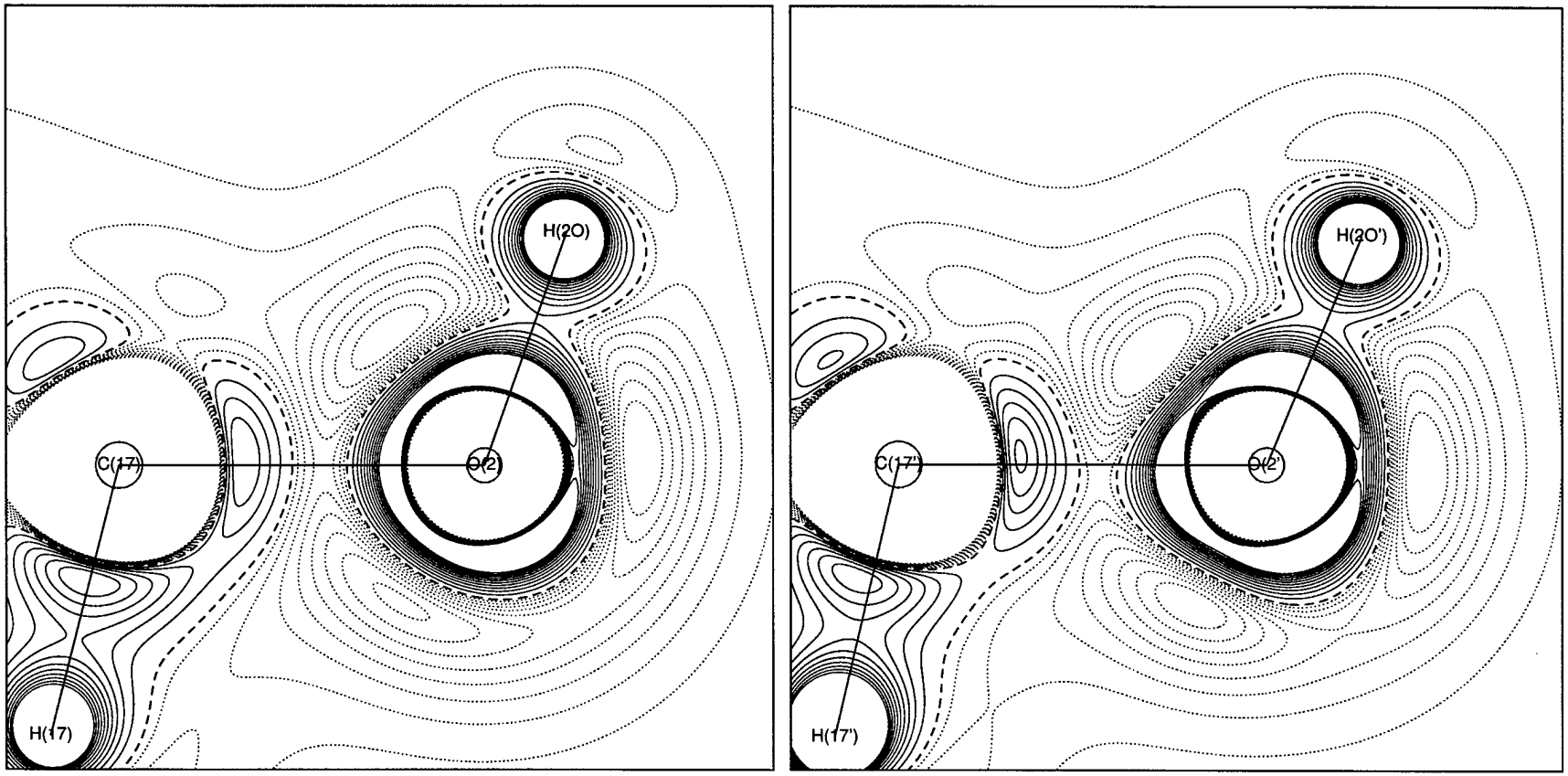

Figure C-22. The Laplacian of the total electron density of atoms at rest in the C17–O2–H2O plane and C17'–O2'–H2O' of 17β-estradiol•½methanol. Contour intervals are 5 eÅ^{-5} starting at 5 eÅ^{-5} (solid blue lines), -2 eÅ^{-5} starting at -2 eÅ^{-5} (dotted red lines), and the dashed line plots 0 eÅ^{-5}.

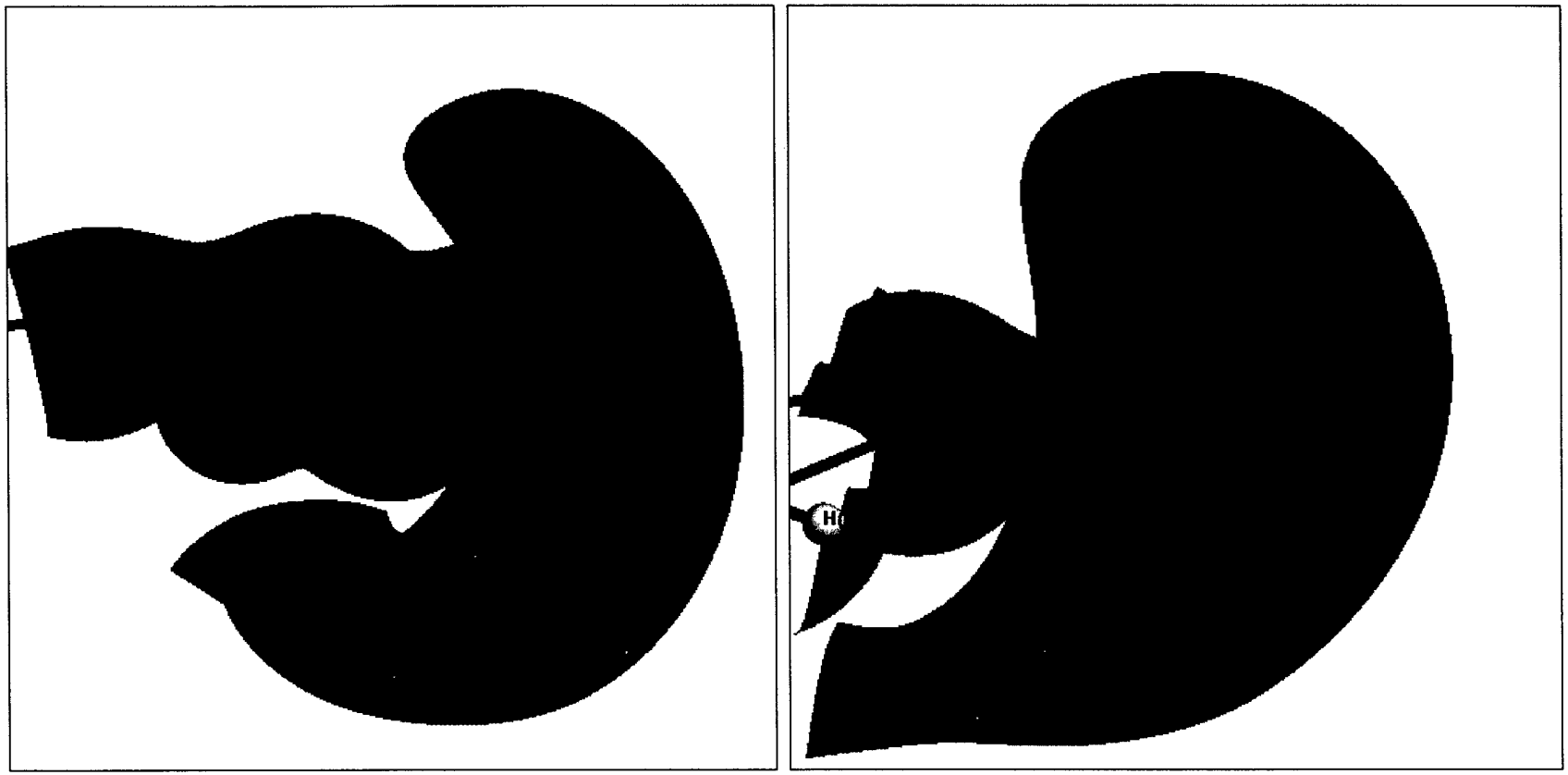

Figure C-23. 17β-estradiol•½methanol, molecule 1 C3 hydroxy, red –0.15 eÅ^{-1}, blue 1.0 eÅ^{-1}.

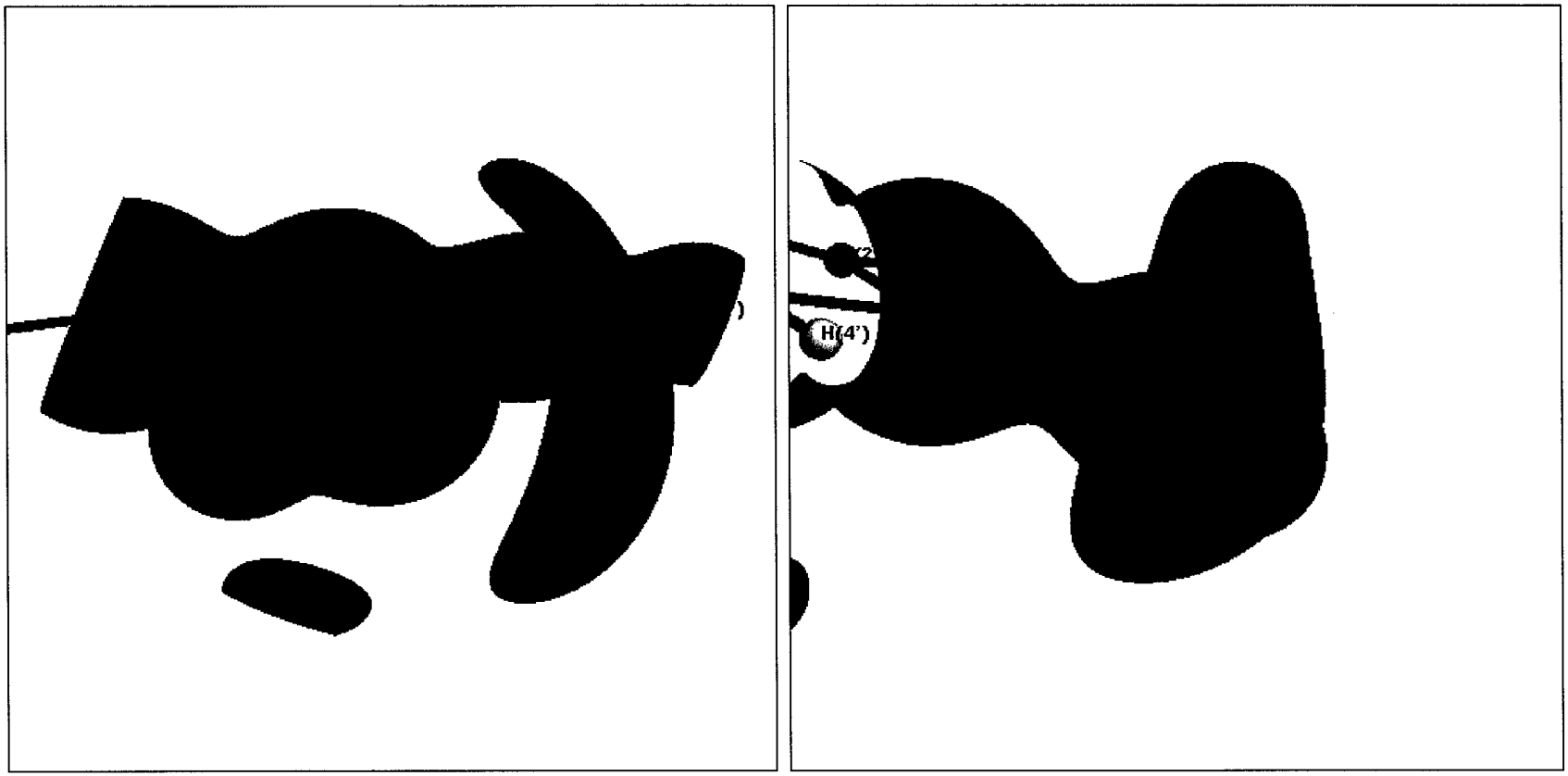

Figure C-24. 17β-estradiol•½methanol, molecule 2 C3' hydroxy, red –0.15 eÅ^{-1}, blue 1.0 eÅ^{-1}.

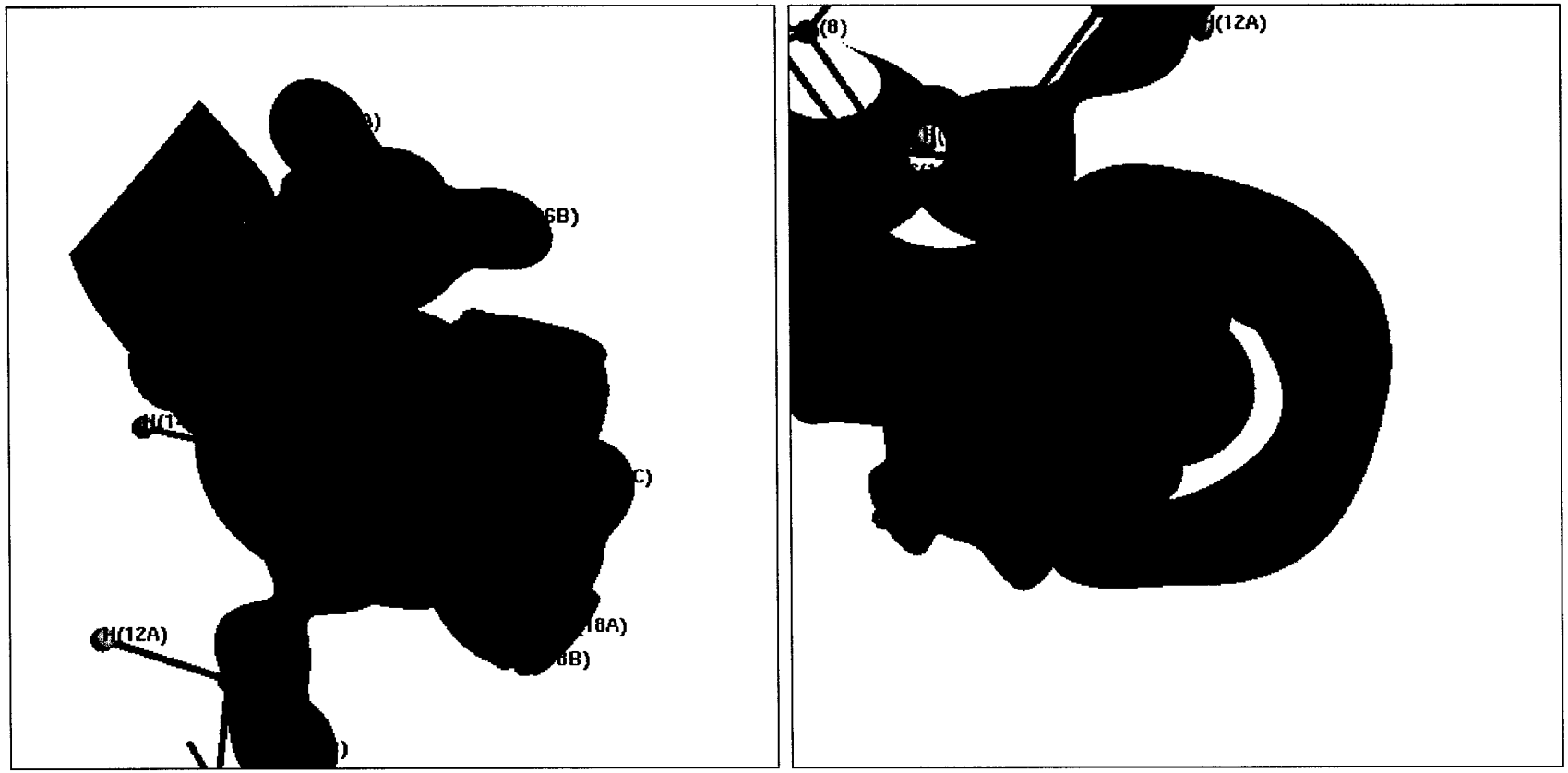

Figure C-25. 17β-estradiol•½methanol, molecule 1 C17 hydroxy, red –0.15 eÅ^{-1}, blue 1.0 eÅ^{-1}.

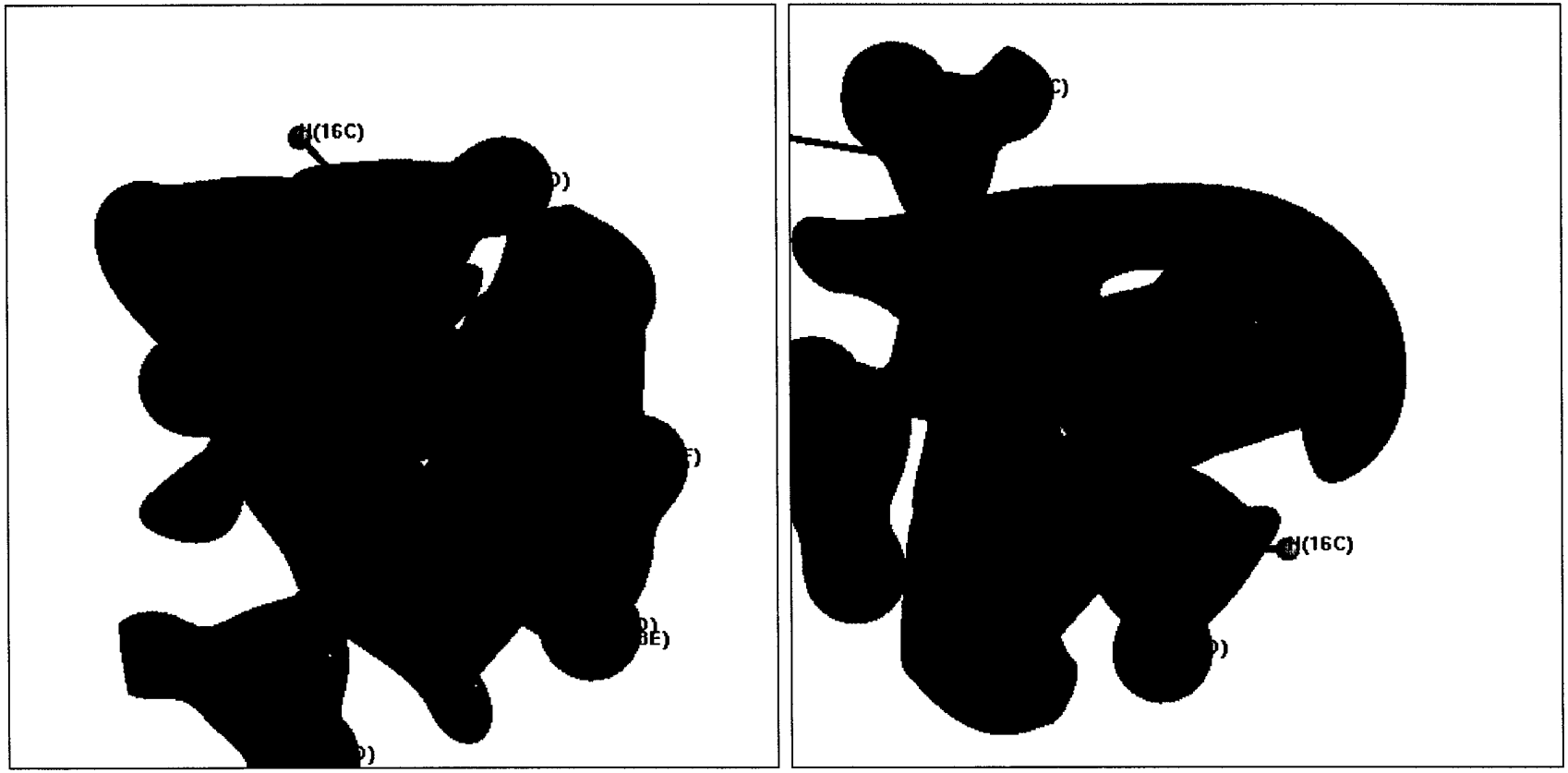

Figure C-26. 17β-estradiol•½methanol, molecule 2 C17' hydroxy, red –0.15 eÅ^{-1}, blue 1.0 eÅ^{-1}.

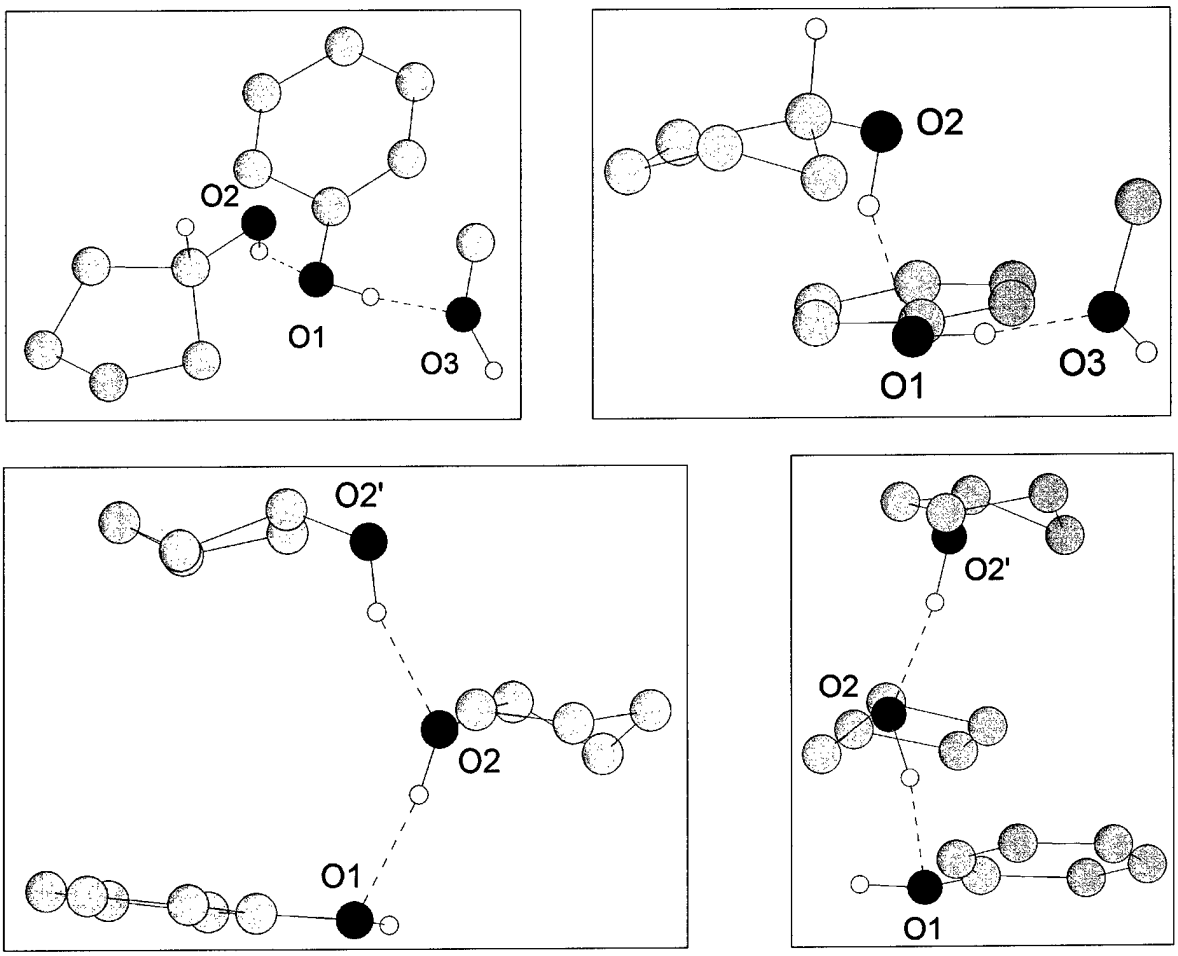

Figure C-27. Geometry of hydrogen bonding interactions of molecule 1 of 17β-estradiol•½methanol.

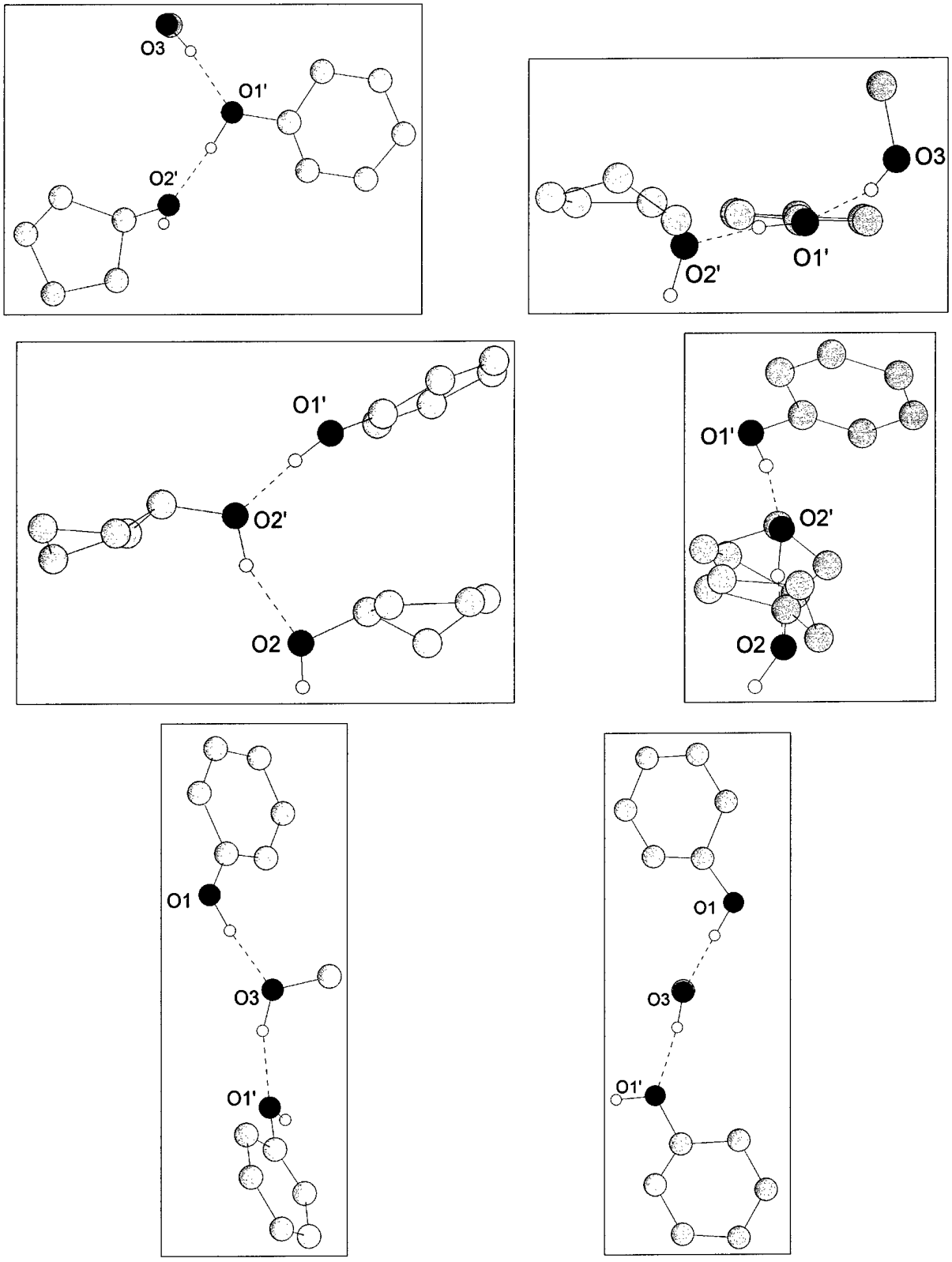

Figure C-28. Geometry of hydrogen bonding interactions of molecule 2 and the methanol of 17β-estradiol•½methanol.

Appendix D
17*a*-estradiol•½H_2O

** Due to the fact the multipole refinement and topological analysis has only recently been completed, some of the figures shown for the previous two structures have not yet been produced for this structure.

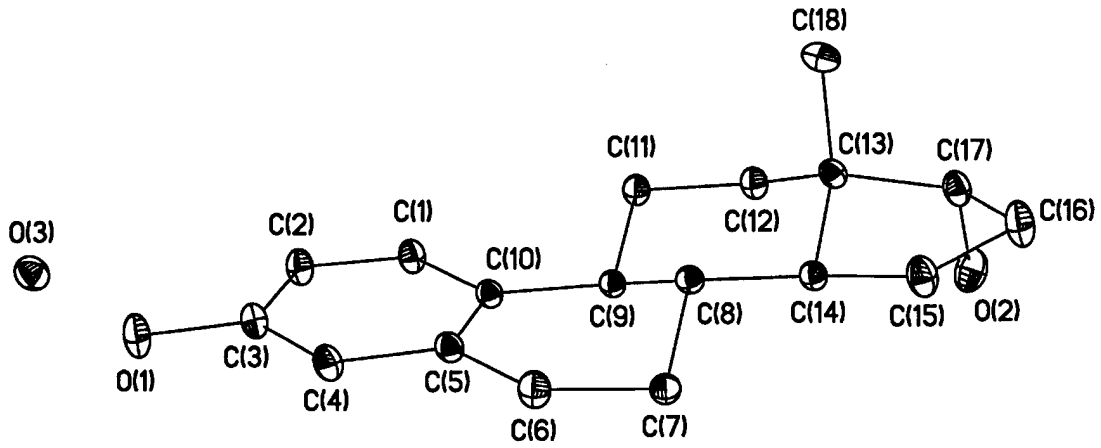

Figure D-1. Thermal ellipsoid plot of 17*a*-estradiol•½H_2O where ellipsoids represent 50% probability electron density of the atom. Hydrogen atoms are omitted for clarity.

Run	2θ	ω	ϕ	Scan Width (°)	# of Frames	Frame Times (sec)
1	0	10	0	-0.30	660	96
2	0	10	90	-0.30	660	96
3	0	10	180	-0.30	660	96
4	0	10	270	-0.30	660	96
5	0	10	0	-0.30	100	96
6	-60	-50	45	-0.30	660	180
7	-60	-50	135	-0.30	660	180
8	-60	-50	225	-0.30	660	180
9	-60	-50	315	-0.30	660	180
10	-60	-50	45	-0.30	100	180

Table D-1. Data collection parameters for 17*a*-estradiol•½H_2O.

Crystal Data			
Chemical Formula	$C_{18}H_{25}O_{2.5}$		
Temperature	100.0(1) K		
Crystal Dimensions	0.24 x 0.33 x 0.33 mm		
Space Group	C2		
A	19.0235(5) Å		
B	7.0653(2) Å		
C	13.3496(3) Å		
β	124.0544(10)		
Volume	1486.56(10) $Å^3$		
Z (Crystallographic)	4		
Integration Parameters			
	Box Size (°)	Profile Fitting (I/σ)	Simple Sum Perimeter Limit
Low Angle	1.2 x 1.2 x 0.8	40 10	0.02
High Angle	1.0 x 1.0 x 0.6	30 10	0.02
Reflection Statistics (from SORTAV)			
Total Reflections	85540		
Rejected Outliers	69		
Unique Reflections	14593		
Average Redundancy	5.9		
Resolution	1.319 $Å^{-1}$		
Completeness	98.2 %		
R_1	3.76 %		
R_2	4.13 %		
R_w	13.52 %		
Z (Refinement)	1.949		

Table D-2. Selected crystal, integration, and reflection data for 17*a*-estradiol•½H_2O.

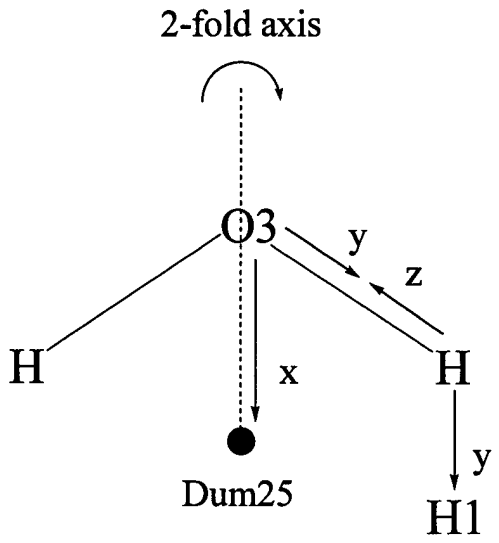

Figure D-2. Coordinate system for the water molecule.

	n	m	$\langle n \rangle$	R_1	R_2	R_w	Z	V
Q < -4	0	0	0.0	0.0000	0.0000	0.0000	0.000	0.000
-4 < Q < -3	0	0	0.0	0.0000	0.0000	0.0000	0.000	0.000
-3 < Q < -2	2	1	2.0	0.3784	0.3657	0.3695	1.086	0.381
-2 < Q < -1	43	14	3.1	0.3661	0.4037	0.4846	0.886	0.368
-1 < Q < 0	1161	326	3.6	1.0974	1.1150	1.0573	1.801	3.167
0 < Q < 1	6088	1550	3.9	0.9922	0.9414	0.9133	2.031	1.676
1 < Q < 2	6618	1657	4.0	0.5715	0.5985	0.5448	2.092	0.650
2 < Q < 3	5241	1299	4.0	0.3530	0.4112	0.3720	2.237	0.386
3 < Q < 4	4586	1054	4.4	0.2565	0.3076	0.2699	2.257	0.277
4 < Q < 6	7017	1516	4.6	0.1805	0.2214	0.1905	2.353	0.195
6 < Q < 8	5775	1128	5.1	0.1290	0.1586	0.1406	2.153	0.141
8 < Q < 10	5187	896	5.8	0.0995	0.1227	0.1095	1.999	0.109
10 < Q < 20	17218	2529	6.8	0.0575	0.0728	0.0725	1.645	0.067
20 < Q < 30	16066	1596	10.1	0.0340	0.0467	0.0399	1.227	0.038
30 < Q < 50	10194	745	13.7	0.0244	0.0340	0.0283	1.235	0.027
50 < Q < 100	144	17	8.5	0.0148	0.0164	0.0170	1.048	0.016
100 < Q	0	0	0.0	0.0000	0.0000	0.0000	0.000	0.000

Table D-3. Intensity-Significance Intervals where n is the number of reflections, m is the number of unique reflections, $\langle n \rangle$ is the average measurement multiplicity, and Q=I/Max ($\sigma_{int}/\sigma_{ext}$) respectively for 17$a$-estradiol•½$H_2O$.

	n	m	$\langle n \rangle$	R_1	R_2	R_w	Z	V
D > 1.029	13550	791	17.1	0.0273	0.0387	0.1137	1.986	0.030
1.029 > D > 0.817	13830	774	17.9	0.0329	0.0362	0.1057	1.817	0.039
0.817 > D > 0.713	6005	743	8.1	0.0362	0.0381	0.1209	2.082	0.041
0.713 > D > 0.648	4332	750	5.8	0.0384	0.0368	0.1320	2.145	0.044
0.648 > D > 0.602	4119	748	5.5	0.0480	0.0463	0.1379	2.182	0.053
0.602 > D > 0.566	3914	749	5.2	0.0565	0.0537	0.1396	2.137	0.064
0.566 > D > 0.538	3668	735	5.0	0.0706	0.0660	0.1467	2.076	0.079
0.538 > D > 0.514	3508	729	4.8	0.0891	0.0866	0.1593	2.163	0.100
0.514 > D > 0.495	3483	752	4.6	0.1057	0.1058	0.1609	2.089	0.116
0.495 > D > 0.478	3201	721	4.4	0.1066	0.1015	0.1629	2.055	0.117
0.478 > D > 0.463	3092	720	4.3	0.1054	0.0935	0.1688	2.063	0.114
0.463 > D > 0.449	3023	728	4.2	0.1491	0.1327	0.1945	2.020	0.163
0.449 > D > 0.438	2820	697	4.0	0.1950	0.1897	0.2191	1.970	0.212
0.438 > D > 0.427	2819	720	3.9	0.2140	0.2053	0.2331	1.947	0.236
0.427 > D > 0.417	2608	686	3.8	0.2517	0.2218	0.2650	2.007	0.280
0.417 > D > 0.408	2594	700	3.7	0.2849	0.2656	0.2784	1.927	0.320
0.408 > D > 0.400	2537	712	3.6	0.3111	0.2877	0.3036	1.932	0.351
0.400 > D > 0.393	2331	678	3.4	0.3549	0.3364	0.3461	1.926	0.405
0.393 > D > 0.386	2277	682	3.3	0.3852	0.3783	0.3658	1.941	0.431
0.386 > D > 0.379	1629	513	3.2	0.4653	0.4655	0.4370	1.769	0.540

Table D-4. Equal-Volume Resolution Shells where n is the number of reflections, m is the number of unique reflections, $\langle n \rangle$ is the average measurement multiplicity, and D=sinθ/λ (Å^{-1}) respectively for 17a-estradiol•½H_2O.

	Monopole	sp^2		sp^3
		20	33+	32-
O1	-0.50			
O2	-0.49			
C1	-0.30	-0.22	0.34	
C2	-0.38	-0.19	0.37	
C3	0.27	-0.21	0.38	
C4	-0.33	-0.17	0.36	
C5	-0.18	-0.22	0.33	
C6	-0.26			0.31
C7	-0.31			0.34
C8	-0.21			0.39
C9	-0.17			0.31
C10	-0.25	-0.18	0.37	
C11	-0.31			0.35
C12	-0.28			0.31
C13	-0.16			0.38
C14	-0.20			0.38
C15	-0.26			0.33
C16	-0.35			0.42
C17	0.20			0.38
C18	-0.32			0.27

	Monopole
H1O	0.40
H2O	0.38
H1	0.23
H2	0.22
H4	0.26
H6x	0.20
H7x	0.17
H8	0.20
H9	0.16
H11x	0.17
H12x	0.16
H14	0.19
H15x	0.16
H16x	0.18
H17	0.13
H18x	0.18

Atoms	Kappa	κ	κ'
O1, O2	1	0.97	1.16
C3	2	1.01	0.92
C17	3	1.02	0.95
C1, C2, C4	4	0.97	0.92
C5, C10	5	0.98	0.87
C6, C7, C8, C9, C11, C12, C13, C14, C15, C16, C17, C18	6	0.98	0.95
all C-H hydrogen atoms	7	1.20	1.29
H1O, H2O	8	1.20	1.29
O3	9		
H3O	10		

Table D-5. Starting values entered into the model for the multipole refinement for 17*a*-estradiol•½H_2O. Units for multipole populations are e^-.

Atom	X	Y	Z
O1	0.11679(1)	0.53051(6)	-0.40619(2)
O2	0.59212(2)	0.40154(6)	0.50812(2)
C1	0.25908(2)	0.32552(6)	-0.10524(2)
C2	0.19311(2)	0.34213(6)	-0.22673(3)
C3	0.18285(2)	0.51139(6)	-0.28726(2)
C4	0.24011(2)	0.65930(6)	-0.22661(2)
C5	0.30786(2)	0.64004(6)	-0.10514(2)
C6	0.37135 (2)	0.80070(6)	-0.04731(3)
C7	0.43341(2)	0.78376(6)	0.08978(2)
C8	0.46397(2)	0.58022(6)	0.12773(2)
C9	0.38729(2)	0.45262(6)	0.09205(2)
C10	0.31740(2)	0.47201(6)	-0.04185(2)
C11	0.41421(2)	0.24647(6)	0.13289(2)
C12	0.48474(2)	0.23044(6)	0.26845(2)
C13	0.56071(2)	0.35552(6)	0.30229(2)
C14	0.52936(2)	0.56082(6)	0.26359(2)
C15	0.61131(2)	0.67896(6)	0.32646(3)
C16	0.67369(2)	0.56827(7)	0.44502(3)
C17	0.62831(2)	0.38263(7)	0.43874(3)
C18	0.60695(2)	0.27766(7)	0.24600(3)
O3	0.00000	0.23142(6)	-0.50000

Atom	X	Y	Z
H1O	0.0858(5)	0.4125(12)	-0.4373(7)
H2O	0.5776(5)	0.2772(12)	0.5221(7)
H1	0.2662(4)	0.1964(10)	-0.0571(6)
H2	0.1501(4)	0.2251(10)	-0.2723(5)
H4	0.2325(4)	0.7893(9)	-0.2743(5)
H6A	0.3381(4)	0.9357(10)	-0.0691(6)
H6B	0.4076(3)	0.7980(8)	-0.0879(5)
H7A	0.4029(3)	0.8300(8)	0.1345(5)
H7B	0.4877(4)	0.8759(9)	0.1198(5)
H8	0.4908(3)	0.5308(8)	0.0777(5)
H9	0.3621(3)	0.5067(8)	0.1432(5)
H11A	0.3595(3)	0.1651(8)	0.1144(4)
H11B	0.4347(3)	0.1816(9)	0.0792(5)
H12A	0.4574(3)	0.2717(8)	0.3184(5)
H12B	0.5030(3)	0.0821(8)	0.2897(5)
H14	0.4967(3)	0.5946(8)	0.3080(5)
H15A	0.6023(4)	0.8213(9)	0.3488(5)
H15B	0.6368(4)	0.6833(10)	0.2710(6)
H16A	0.6891(4)	0.6405(10)	0.5271(6)
H16B	0.7310(4)	0.5301(10)	0.4497(6)
H17	0.6733(3)	0.2639(8)	0.4791(4)
H18A	0.6315(4)	0.1412(9)	0.2813(6)
H18B	0.6599(4)	0.3615(11)	0.2676(6)
H18C	0.5672(4)	0.2631(10)	0.1507(5)
H3O	-0.0329(6)	0.1294(14)	-0.4989(8)

Table D-6. Fractional atomic coordinates for 17*a*-estradiol•½H_2O.

Atom	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.01474(8)	0.01787(9)	0.01159(8)	-0.00278(7)	0.00232(7)	0.00226(7)
O2	0.02309(10)	0.02411(11)	0.01353(9)	-0.00461(9)	0.00994(8)	-0.00101(8)
C1	0.01204(9)	0.01148(9)	0.01149(9)	-0.00201(7)	0.00414(8)	0.00130(7)
C2	0.01229(9)	0.01414(10)	0.01165(9)	-0.00233(8)	0.00411(8)	0.00150(8)
C3	0.01088(9)	0.01535(10)	0.01028(9)	-0.00064(7)	0.00421(7)	0.00195(8)
C4	0.01196(9)	0.01291(9)	0.01167(9)	0.00007(7)	0.00481(8)	0.00282(7)
C5	0.01117(8)	0.00945(8)	0.01079(8)	0.00050(7)	0.00505(7)	0.00167(7)
C6	0.01588(10)	0.00952(8)	0.01253(9)	-0.00106(7)	0.00521(8)	0.00213(7)
C7	0.01282(9)	0.00788(8)	0.01220(9)	-0.00003(7)	0.00565(8)	0.00038(7)
C8	0.01065(8)	0.00806(7)	0.01068(8)	0.00034(6)	0.00579(7)	0.00082(6)
C9	0.01013(8)	0.00851(8)	0.01017(8)	0.00023(6)	0.00513(7)	0.00084(6)
C10	0.01026(8)	0.00922(8)	0.01016(8)	0.00013(6)	0.00499(7)	0.00115(6)
C11	0.01317(9)	0.00837(8)	0.01196(9)	-0.00036(7)	0.00511(8)	0.00119(7)
C12	0.01257(9)	0.01020(8)	0.01198(9)	-0.00066(7)	0.00537(8)	0.00224(7)
C13	0.01036(8)	0.01021(8)	0.01170(9)	0.00115(7)	0.00540(7)	0.00168(7)
C14	0.01012(8)	0.00939(8)	0.01077(8)	-0.00013(6)	0.00488(7)	0.00063(7)
C15	0.01293(9)	0.01331(10)	0.01594(10)	-0.00301(8)	0.00472(8)	0.00240(8)
C16	0.01292(10)	0.01801(11)	0.01616(11)	-0.00385(9)	0.00231(9)	0.00290(9)
C17	0.01204(9)	0.01325(9)	0.01289(9)	0.00060(7)	0.00418(8)	0.00286(8)
C18	0.01651(11)	0.01638(11)	0.02061(12)	0.00425(9)	0.01234(10)	0.00207(9)
O3	0.01581(12)	0.01773(13)	0.02136(14)	0.00000	0.00928(11)	0.00000

Table D-7. Anisotropic thermal parameters of non-H atoms for 17*a*-estradiol•½H_2O.

Atom	U_{iso}
H1O	0.0386(18)
H2O	0.0471(20)
H1	0.0519(16)
H2	0.0460(14)
H4	0.0447(14)
H6A	0.0564(15)
H6B	0.0449(13)
H7A	0.0413(13)
H7B	0.0434(12)
H8	0.0380(12)
H9	0.0392(12)
H11A	0.0436(13)
H11B	0.0464(13)
H12A	0.0410(12)
H12B	0.0445(13)

Atom	U_{iso}
H14	0.0407(12)
H15A	0.0470(13)
H15B	0.0550(15)
H16A	0.0586(16)
H16B	0.0598(16)
H17	0.0426(12)
H18A	0.0577(15)
H18B	0.0644(17)
H18C	0.0538(14)
H3O	0.1065(51)

Table D-8. Isotropic thermal parameters of H atoms for 17*a*-estradiol•½H_2O.

Atoms	Bond Length (Å)
O1 – C3	1.3724(3)
O2 – C17	1.4365(4)
C1 – C2	1.3927(4)
C1 – C10	1.4024(4)
C2 – C3	1.3945(4)
C3 – C4	1.3951(4)
C4 – C5	1.4030(3)
C5 – C6	1.5162(4)
C5 – C10	1.4087(3)
C6 – C7	1.5289(4)
C7 – C8	1.5274(3)
C8 – C9	1.5457(3)
C8 – C14	1.5261(3)

Atoms	Bond Length (Å)
C9 – C10	1.5232(3)
C9 – C11	1.5390(3)
C11 – C12	1.5390(4)
C12 – C13	1.5305(4)
C13 – C14	1.5432(3)
C13 – C17	1.5444(4)
C13 – C18	1.5431(4)
C14 – C15	1.5382(4)
C15 – C16	1.5560(4)
C16 – C17	1.5465(4)

Table D-9. Bond distances of non-H atoms of 17*a*-estradiol•½H_2O.

Atoms	Bond Angle (°)
C3 – O1 – H1O	110.8(5)
C17 – O2 – H2O	109.3(5)
C2 – C1 – C10	122.2(1)
C2 – C1 – H1	119.7(4)
C10 – C1 – H1	118.1(4)
C1 – C2 – C3	119.3(1)
C1 – C2 – H2	119.7(4)
C3 – C2 – H2	120.9(4)
O1 – C3 – C2	119.7(1)
O1 – C3 – C4	120.6(1)
C2 – C3 – C4	119.7(1)
C3 – C4 – C5	120.8(1)
C3 – C4 – H4	119.5(4)
C5 – C4 – H4	119.8(4)
C4 – C5 – C6	118.0(1)
C4 – C5 – C10	120.1(1)
C6 – C5 – C10	121.8(1)
C5 – C6 - C7	114.3(1)
C5 – C6 – H6A	110.0(4)
C5 – C6 – H6B	106.2(3)
C7 – C6 – H6A	109.3(4)
C7 – C6 – H6B	108.3(3)
H6A – C6 – H6B	108.5(5)
C6 – C7 – C8	111.5(1)
C6 – C7 – H7A	109.9(3)
C6 – C7 – H7B	109.3(3)
C8 – C7 – H7A	108.7(3)
C8 – C7 – H7B	109.5(4)
H7A – C7 – H7B	107.8(4)
C7 – C8 – C9	109.2(1)
C7 – C8 – C14	112.6(1)

Atoms	Bond Angle (°)
C9 – C8 – C14	108.3(1)
C7 – C8 – H8	108.5(4)
C9 – C8 – H8	107.8(3)
C14 – C8 – H8	110.3(3)
C8 – C9 – C10	111.2(1)
C8 – C9 – C11	111.9(1)
C10 – C9 – C11	113.5(1)
C8 – C9 – H9	105.7(3)
C10 – C9 – H9	107.5(3)
C11 – C9 – H9	106.4(4)
C1 – C10 – C5	117.9(1)
C1 – C10 – C9	121.2(1)
C5 – C10 – C9	120.9(1)
C9 – C11 – C12	112.6(1)
C9 – C11 – H11A	109.4(3)
C9 – C11 – H11B	109.6(4)
C12 – C11 – H11A	108.7(3)
C12 – C11 – H11B	110.2(3)
H11A – C11 – H11B	106.1(5)
C11 – C12 – C13	111.2(1)
C11 – C12 – H12A	107.4(3)
C11 – C12 – H12B	108.5(3)
C13 – C12 – H12A	111.1(3)
C13 – C12 – H12B	111.6(3)
H12A – C12 – H12B	106.8(5)
C12 – C13 – C14	108.7(1)
C12 – C13 – C17	116.4(1)
C12 – C13 – C18	110.6(1)
C14 – C13 – C17	100.9(1)
C14 – C13 – C18	113.0(1)
C17 – C13 – C18	107.1(1)

Atoms	Bond Angle (°)
C8 – C14 – C13	112.8(1)
C8 – C14 – C15	120.2(1)
C13 – C14 – C15	104.1(1)
C8 – C14 – H14	106.9(3)
C13 – C14 – H14	104.6(3)
C15 – C14 – H14	107.1(3)
C14 – C15 – C16	104.2(1)
C14 – C15 – H15A	112.5(3)
C14 – C15 – H15B	110.2(4)
C16 – C15 – H15A	109.4(3)
C16 – C15 – H15B	109.2(4)
H15A – C15 – H15B	111.0(5)
C15 – C16 – C17	106.7(1)
C15 – C16 – H16A	114.2(4)
C15 – C16 – H16B	110.6(4)
C17 – C16 – H16A	106.2(4)
C17 – C16 – H16B	107.6(4)
H16A – C16 – H16B	111.1(5)
O2 – C17 – C13	112.9(1)
O2 – C17 – C16	109.9(1)
C13 – C17 – C16	103.9(1)
O2 – C17 – H17	106.1(3)
C13 – C17 – H17	112.9(3)
C16 – C17 – H17	111.3(3)
C13 – C18 – H18A	109.8(4)
C13 – C18 – H18B	112.5(4)
C13 – C18 – H18C	113.7(4)
H18A – C18 – H18B	105.8(6)
H18A – C18 – H18C	106.6(6)
H18B – C18 – H18C	108.1(5)
H3O – O3 – H3O'	82.7(10)

Table D-10. Bond angles of 17*a*-estradiol•½H_2O.

Atom	Monopole Population ($P_{0,0}$)
O1	6.519(12)
O2	6.526(12)
C1	4.222(23)
C2	4.254(22)
C3	3.855(20)
C4	4.247(22)
C5	4.127(21)
C6	4.217(22)
C7	4.217(21)
C8	4.127(21)
C9	4.122(21)
C10	4.101(21)
C11	4.226(20)
C12	4.236(20)
C13	4.189(22)
C14	4.121(22)
C15	4.308(21)
C16	4.302(21)
C17	3.849(19)
C18	4.379(22)
O3	3.274(8)

Atom	Monopole Population ($P_{0,0}$)
H1O	0.621(11)
H2O	0.611(11)
H1	0.780(11)
H2	0.788(10)
H4	0.783(11)
H6A	0.853(9)
H6B	0.853(9)
H7A	0.854(7)
H7B	0.854(7)
H8	0.818(10)
H9	0.821(10)
H11A	0.858(8)
H11B	0.858(8)
H12A	0.852(8)
H12B	0.852(8)
H14	0.844(11)
H15A	0.853(8)
H15B	0.853(8)
H16A	0.851(9)
H16B	0.851(9)
H17	0.908(10)
H18A	0.879(7)
H18B	0.879(7)
H18C	0.879(7)
H3O	0.726(8)

Table D-11. Monopole populations (e^-) of 17*a*-estradiol•½H_2O.

Multipoles	O1	O2	O3
$P_{1,+1}$	-0.011(7)	-0.036(7)	0.0
$P_{1,-1}$	0.020(11)	0.030(11)	0.048(10)
$P_{1,0}$	0.029(8)	0.014(6)	0.0
$P_{2,0}$	0.096(7)	0.083(7)	0.0
$P_{2,+1}$	-0.037(6)	-0.016(6)	0.0
$P_{2,-1}$	-0.035(7)	-0.046(7)	0.0
$P_{2,+2}$	-0.064(7)	-0.021(7)	0.0
$P_{2,-2}$	0.022(7)	0.065(7)	0.0
$P_{3,0}$	0.014(12)	-0.040(9)	0.0
$P_{3,+1}$	-0.015(9)	-0.081(8)	0.0
$P_{3,-1}$	0.029(12)	-0.017(13)	0.0
$P_{3,+2}$	0.026(10)	-0.016(9)	0.0
$P_{3,-2}$	0.022(11)	0.089(13)	0.0
$P_{3,+3}$	0.124(8)	0.077(9)	-0.100(7)
$P_{3,-3}$	0.020(11)	-0.042(14)	0.0
$P_{4,0}$	0.0	-0.080(11)	0.0
$P_{4,+1}$	0.0	0.034(10)	0.0
$P_{4,-1}$	0.0	0.0	0.0
$P_{4,+2}$	0.0	0.011(10)	0.0
$P_{4,-2}$	-0.018(10)	0.021(11)	0.0
$P_{4,+3}$	-0.062(10)	0.032(10)	0.0
$P_{4,-3}$	0.0	0.047(11)	0.0
$P_{4,+4}$	0.018(9)	-0.023(10)	-0.059(6)
$P_{4,-4}$	-0.090(10)	-0.071(11)	0.0

Table D-12. Multipole populations (e^-) of Oxygen and Nitrogen atoms of 17*a*-estradiol•½H_2O.

Multipoles	C1	C2	C3	C4	C5	C6	C7	C8	C9
$P_{1,+1}$	-0.048(11)	-0.153(16)	-0.089(14)	0.047(12)	0.186(16)	0.114(15)	0.108(14)	-0.019(11)	-0.021(11)
$P_{1,-1}$	-0.074(16)	-0.041(13)	0.155(13)	0.172(17)	0.104(13)	0.0	-0.027(11)	-0.131(13)	0.122(14)
$P_{1,0}$	0.073(11)	0.075(11)	0.091(12)	0.064(11)	0.0	0.023(11)	-0.119(12)	-0.103(13)	0.0
$P_{2,0}$	-0.242(9)	-0.175(10)	-0.226(9)	-0.171(10)	-0.250(10)	-0.021(9)	-0.028(9)	0.039(9)	0.0
$P_{2,+1}$	0.035(9)	0.066(10)	-0.017(10)	0.0	0.0	-0.010(9)	0.023(9)	-0.018(9)	0.0
$P_{2,-1}$	0.0	0.0	-0.039(9)	-0.011(10)	0.012(9)	0.038(9)	0.0	0.0	0.018(8)
$P_{2,+2}$	0.011(10)	0.035(10)	0.067(11)	0.0	0.031(11)	0.0	0.036(8)	-0.027(8)	0.017(8)
$P_{2,-2}$	-0.063(10)	-0.055(10)	-0.013(10)	-0.055(11)	-0.018(11)	-0.069(9)	0.010(9)	0.029(9)	0.0
$P_{3,0}$	-0.050(17)	-0.026(16)	-0.070(17)	-0.064(16)	0.0	-0.018(16)	0.0	0.103(14)	0.223(15)
$P_{3,+1}$	0.0	0.0	0.060(13)	0.0	0.023(14)	-0.085(12)	-0.085(12)	0.054(15)	0.105(14)
$P_{3,-1}$	0.022(14)	-0.019(13)	0.044(13)	-0.027(13)	0.015(14)	-0.046(13)	0.096(13)	0.124(15)	0.128(12)
$P_{3,+2}$	0.029(15)	0.0	-0.050(16)	0.019(14)	0.0	0.048(15)	-0.029(14)	-0.187(15)	0.025(15)
$P_{3,-2}$	0.018(14)	-0.020(15)	0.028(15)	0.0	-0.049(17)	0.170(14)	0.313(15)	0.301(11)	0.145(12)
$P_{3,+3}$	0.310(12)	0.293(12)	0.301(13)	0.288(13)	0.334(14)	-0.222(14)	-0.082(13)	0.081(12)	0.122(13)
$P_{3,-3}$	0.0	0.0	-0.124(18)	0.039(16)	-0.045(18)	0.059(13)	-0.048(14)	-0.027(13)	-0.111(14)

Multipoles	C10	C11	C12	C13	C14	C15	C16	C17	C18
$P_{1,+1}$	0.085(16)	-0.108(13)	-0.069(12)	0.0	0.128(13)	0.097(16)	0.109(12)	-0.028(10)	0.138(11)
$P_{1,-1}$	-0.142(14)	0.109(13)	-0.056(13)	-0.084(13)	-0.069(11)	0.0	-0.171(13)	0.0	0.0
$P_{1,0}$	0.026(12)	0.044(11)	0.129(12)	-0.123(12)	-0.123(12)	0.090(11)	-0.101(11)	-0.148(13)	-0.150(12)
$P_{2,0}$	-0.168(10)	0.0	-0.019(10)	-0.031(10)	-0.012(9)	-0.086(10)	0.0	0.046(9)	-0.024(10)
$P_{2,+1}$	0.0	-0.023(8)	0.0	0.046(9)	0.032(9)	-0.019(9)	-0.027(9)	0.018(9)	0.027(9)
$P_{2,-1}$	0.073(10)	-0.035(9)	0.010(8)	-0.018(9)	-0.010(9)	-0.031(9)	0.026(10)	0.055(9)	0.045(9)
$P_{2,+2}$	-0.042(11)	-0.027(9)	0.025(9)	-0.018(9)	-0.064(9)	0.086(8)	0.039(10)	-0.024(8)	-0.047(8)
$P_{2,-2}$	-0.050(10)	-0.041(8)	0.035(8)	-0.014(9)	0.034(9)	-0.016(9)	0.019(9)	-0.021(8)	0.041(9)
$P_{3,0}$	-0.058(18)	0.046(15)	0.055(15)	0.062(15)	0.021(15)	0.0	0.023(13)	-0.038(15)	0.029(14)
$P_{3,+1}$	-0.028(13)	-0.110(13)	-0.171(14)	0.0	-0.018(11)	-0.143(12)	-0.071(13)	0.067(13)	0.058(15)
$P_{3,-1}$	-0.019(14)	0.024(14)	-0.037(14)	0.119(13)	0.103(13)	-0.032(13)	0.042(15)	0.054(15)	0.160(14)
$P_{3,+2}$	-0.098(16)	0.104(14)	-0.051(12)	-0.130(15)	-0.058(13)	0.0	-0.106(16)	0.050(14)	-0.086(14)
$P_{3,-2}$	-0.024(16)	0.280(13)	0.201(13)	0.335(12)	0.327(14)	0.273(14)	0.288(13)	0.283(13)	0.134(12)
$P_{3,+3}$	0.361(14)	-0.110(14)	-0.134(13)	0.051(13)	-0.034(13)	-0.206(15)	-0.082(15)	0.048(11)	0.215(12)
$P_{3,-3}$	0.045(18)	0.099(12)	0.015(13)	-0.117(14)	-0.027(13)	0.036(14)	-0.081(11)	-0.018(12)	-0.117(13)

Table D-13. Multipole populations (e^-) of Carbon atoms of 17*a*-estradiol•½H_2O.

Atoms	$P_{1,0}$	$P_{2,0}$
H1O	0.155(14)	0.021(18)
H2O	0.290(15)	0.033(19)
H1	0.128(15)	0.023(19)
H2	0.186(14)	0.038(18)
H4	0.161(14)	0.041(17)
H6A	0.192(9)	0.026(11)
H6B	0.192(9)	0.026(11)
H7A	0.140(8)	0.041(10)
H7B	0.140(8)	0.041(10)
H8	0.139(11)	0.0
H9	0.107(11)	0.015(15)
H11A	0.135(8)	0.057(12)
H11B	0.135(8)	0.057(12)
H12A	0.159(8)	0.043(10)
H12B	0.159(8)	0.043(10)
H14	0.107(13)	0.038(17)
H15A	0.165(9)	0.0
H15B	0.165(9)	0.0
H16A	0.183(9)	0.031(11)
H16B	0.183(9)	0.031(11)
H17	0.193(13)	0.0
H18A	0.134(7)	-0.018(9)
H18B	0.134(7)	-0.018(9)
H18C	0.134(7)	-0.018(9)
H3O	0.141(16)	0.035(23)

Table D-14. Multipole populations (e^-) of Hydrogen atoms of 17*a*-estradiol•½H_2O.

Bond	$\rho(r_c)$	$\nabla^2\rho(r_c)$	R_{ij}	d_1	d_2	λ_1	λ_2	λ_3	ε
O1 – C3	2.120	-15.427	1.3757	0.8070	0.5687	-17.48	-15.51	17.57	0.13
O1 – H1O	2.170	-24.028	0.9703	0.7454	0.2249	-33.19	-32.56	41.72	0.02
O2 – C17	1.727	-5.757	1.4367	0.8340	0.6027	-11.99	-11.06	17.30	0.08
O2 – H2O	2.370	-37.913	0.9701	0.7433	0.2267	-37.48	-36.47	36.04	0.03
C1 – C2	2.237	-21.462	1.3953	0.6846	0.7107	-16.78	-14.23	9.54	0.18
C1 – C10	2.179	-20.448	1.4025	0.7211	0.6814	-16.21	-13.30	9.06	0.22
C1 – H1	1.993	-17.855	1.0801	0.6682	0.4119	-18.44	-17.63	18.22	0.05
C2 – C3	2.127	-19.668	1.3965	0.6541	0.7424	-16.14	-13.30	9.77	0.21
C2 – H2	2.059	-19.553	1.0801	0.6492	0.4309	-18.84	-17.27	16.56	0.09
C3 – C4	2.195	-20.099	1.3957	0.6645	0.7313	-17.10	-13.55	10.55	0.26
C4 – C5	2.158	-19.740	1.4048	0.7200	0.6848	-15.80	-13.25	9.31	0.19
C4 – H4	1.797	-16.893	1.0805	0.6243	0.4562	-16.36	-14.58	14.04	0.12
C5 – C6	1.679	-11.363	1.5163	0.7319	0.7844	-11.53	-10.13	10.30	0.14
C5 – C10	2.165	-21.077	1.4113	0.7604	0.6510	-16.47	-13.10	8.49	0.26
C6 – C7	1.728	-10.606	1.5301	0.7886	0.7415	-11.40	-10.59	11.38	0.08
C6 – H6A	1.791	-13.393	1.0901	0.6155	0.4747	-15.37	-12.82	14.79	0.20
C6 – H6B	1.812	-13.339	1.0906	0.6185	0.4721	-15.23	-13.08	14.97	0.16
C7 – C8	1.692	-11.578	1.5280	0.8049	0.7231	-11.55	-10.52	10.49	0.10
C7 – H7A	1.949	-17.580	1.0902	0.6472	0.4431	-17.72	-16.49	16.63	0.07
C7 – H7B	1.778	-14.845	1.0901	0.6271	0.4631	-14.99	-14.84	14.99	0.01
C8 – C9	1.630	-9.845	1.5468	0.8050	0.7419	-10.55	-10.01	10.72	0.05
C8 – C14	1.667	-11.245	1.5278	0.7631	0.7647	-11.17	-10.58	10.50	0.06
C8 – H8	1.880	-14.232	1.1000	0.6681	0.4319	-16.32	-15.97	18.06	0.02
C9 – C10	1.700	-10.657	1.5255	0.7407	0.7848	-11.32	-9.98	10.65	0.13
C9 – C11	1.645	-10.410	1.5394	0.7939	0.7456	-10.79	-10.30	10.68	0.05
C9 – H9	1.825	-14.327	1.1002	0.6682	0.4320	-16.31	-15.61	17.60	0.04

Table D-15. Topological properties of bond critical points in 17*a*-estradiol•½H_2O.

Bond	$\rho(r_c)$	$\nabla^2\rho(r_c)$	R_{ij}	d_1	d_2	λ_1	λ_2	λ_3	ε
C11 – C12	1.550	-8.036	1.5406	0.7751	0.7655	-9.84	-9.04	10.84	0.09
C11 – H11A	2.023	-18.370	1.0906	0.6579	0.4326	-18.66	-17.46	17.74	0.07
C11 – H11B	1.965	-16.884	1.0901	0.6517	0.4383	-17.38	-16.77	17.27	0.04
C12 – C13	1.717	-10.751	1.5339	0.7449	0.7889	-10.95	-10.88	11.08	0.01
C12 – H12A	1.890	-16.414	1.0902	0.6346	0.4556	-16.38	-15.72	15.69	0.04
C12 – H12B	2.031	-17.189	1.0903	0.6553	0.4350	-17.75	-17.29	17.85	0.03
C13 – C14	1.632	-9.730	1.5434	0.7366	0.8068	-10.29	-10.06	10.61	0.02
C13 – C17	1.647	-8.917	1.5507	0.7879	0.7628	-11.22	-9.62	11.93	0.17
C13 – C18	1.688	-10.826	1.5436	0.7674	0.7762	-11.27	-10.57	11.02	0.07
C14 – C15	1.647	-9.329	1.5399	0.7335	0.8064	-10.51	-9.95	11.14	0.06
C14 – H14	1.825	-14.820	1.1001	0.6597	0.4403	-16.15	-15.66	16.99	0.03
C15 – C16	1.592	-9.009	1.5578	0.8083	0.7495	-10.37	-9.69	11.05	0.07
C15 – H15A	1.830	-15.696	1.0910	0.6296	0.4613	-16.67	-14.53	15.51	0.15
C15 – H15B	1.918	-15.537	1.0908	0.6429	0.4478	-17.05	-15.35	16.86	0.11
C16 – C17	1.695	-10.605	1.5467	0.8271	0.7196	-11.51	-10.72	11.63	0.07
C16 – H16A	1.889	-16.413()	1.0901	0.6256	0.4644	-16.48	-14.99	15.05	0.10
C16 – H16B	1.918	-15.979()	1.0906	0.6336	0.4570	-16.06	-15.91	15.98	0.01
C17 – H17	1.975	-15.631	1.1004	0.6469	0.4535	-17.73	-16.64	18.74	0.07
C18 – H18A	2.060	-16.196	1.0601	0.6334	0.4267	-18.22	-16.43	18.45	0.11
C18 – H18B	1.851	-13.606	1.0638	0.6195	0.4443	-16.56	-14.36	17.31	0.15
C18 – H18C	1.910	-13.904	1.0605	0.6196	0.4408	-17.12	-14.02	17.24	0.22
O3 – H3O	2.413	-67.609	0.9607	0.7967	0.1640	-51.40	-48.06	31.85	0.07

Table D-16. Topological properties of bond critical points in 17*a*-estradiol•½H_2O continued.

Bond	$\rho(r_c)$	$\nabla^2\rho(r_c)$	R_{ij}	d_1	d_2	λ_1	λ_2	λ_3	ε
O1—H1O··O3	0.124	3.237	1.8746	1.2378	0.6367	-0.75	-0.68	4.67	0.11
O2—H2O··O1	0.094	2.431	2.0909	0.7521	1.3388	-0.70	-0.47	3.60	0.49
O3—H3O··O2	0.165	2.371	1.9303	0.6247	1.3056	-0.99	-0.92	4.28	0.08

Table D-17. Topological properties of bond critical points in the hydrogen bonds of 17*a*-estradiol•½H_2O.

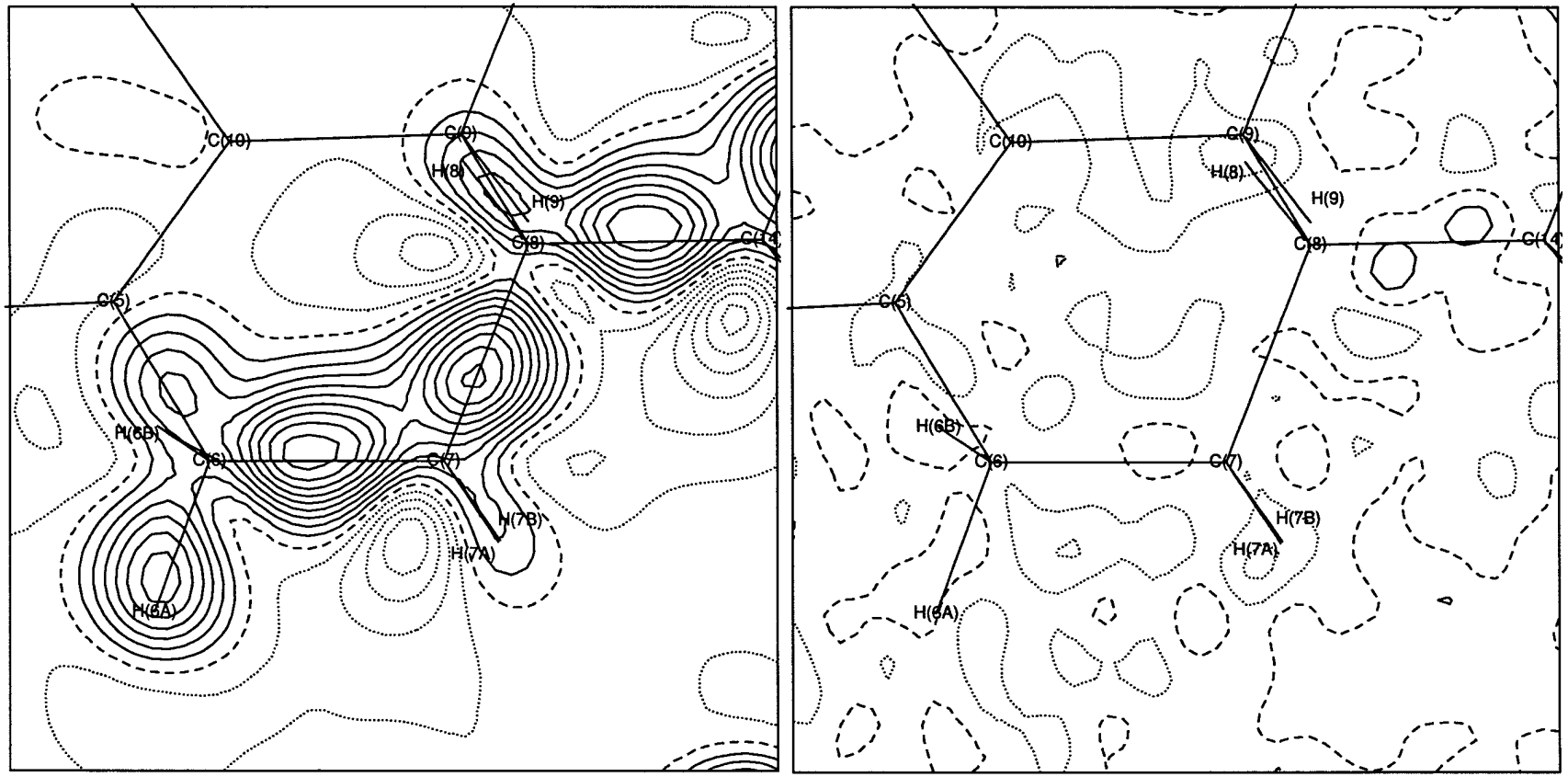

Figure D-3. Dynamic model map and residual map in the C6 – C7 – C8 plane of 17*a*-estradiol•½H_2O. Contour intervals are 0.05 e$Å^{-3}$ with solid lines positive, dashed lines zero, and dotted lines negative.

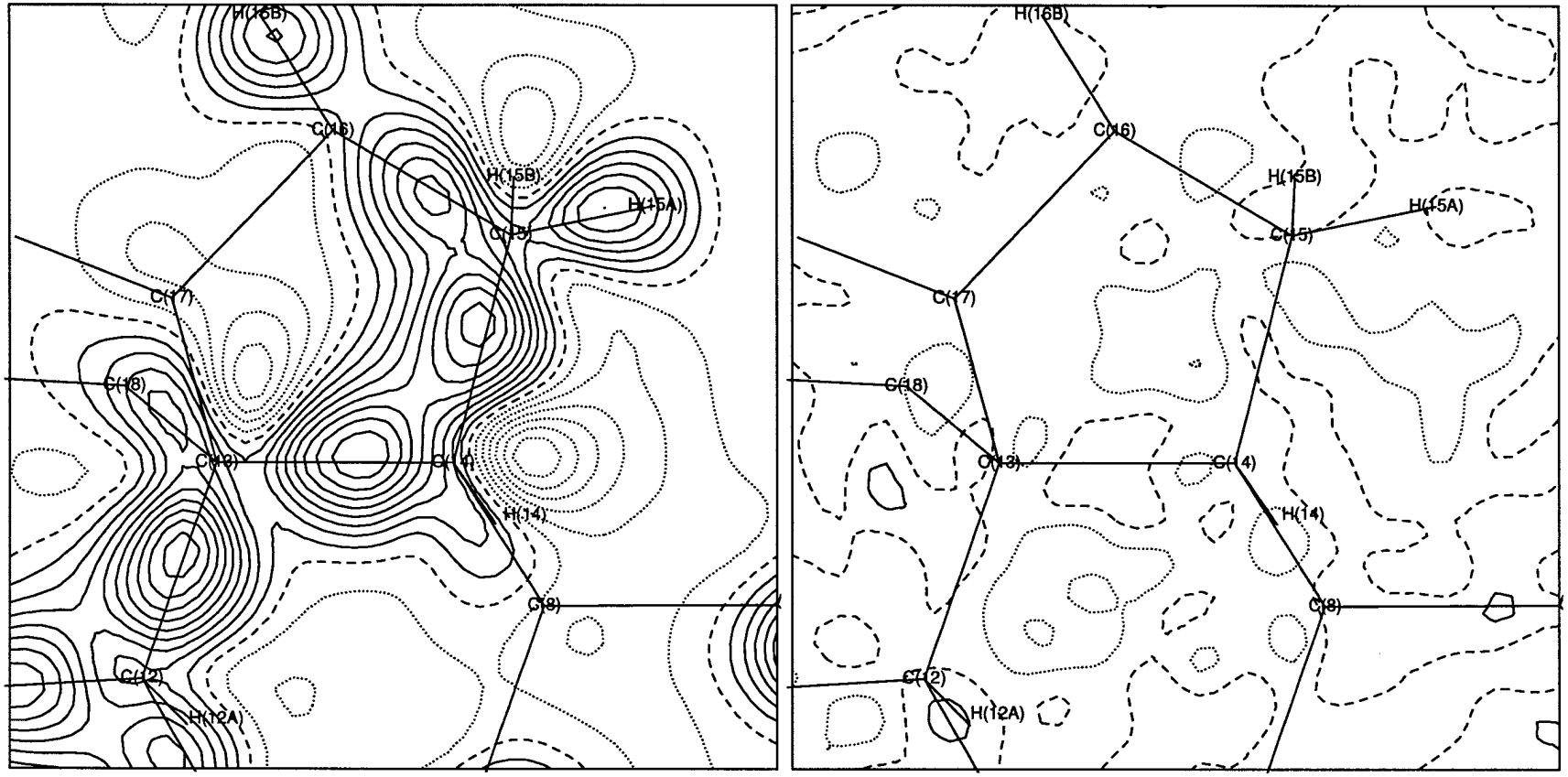

Figure D-4. Dynamic model map and residual map in the C13 – C14 – C15 plane of 17*a*-estradiol•½H_2O. Contour intervals are 0.05 e$Å^{-3}$ with solid lines positive, dashed lines zero, and dotted lines negative.

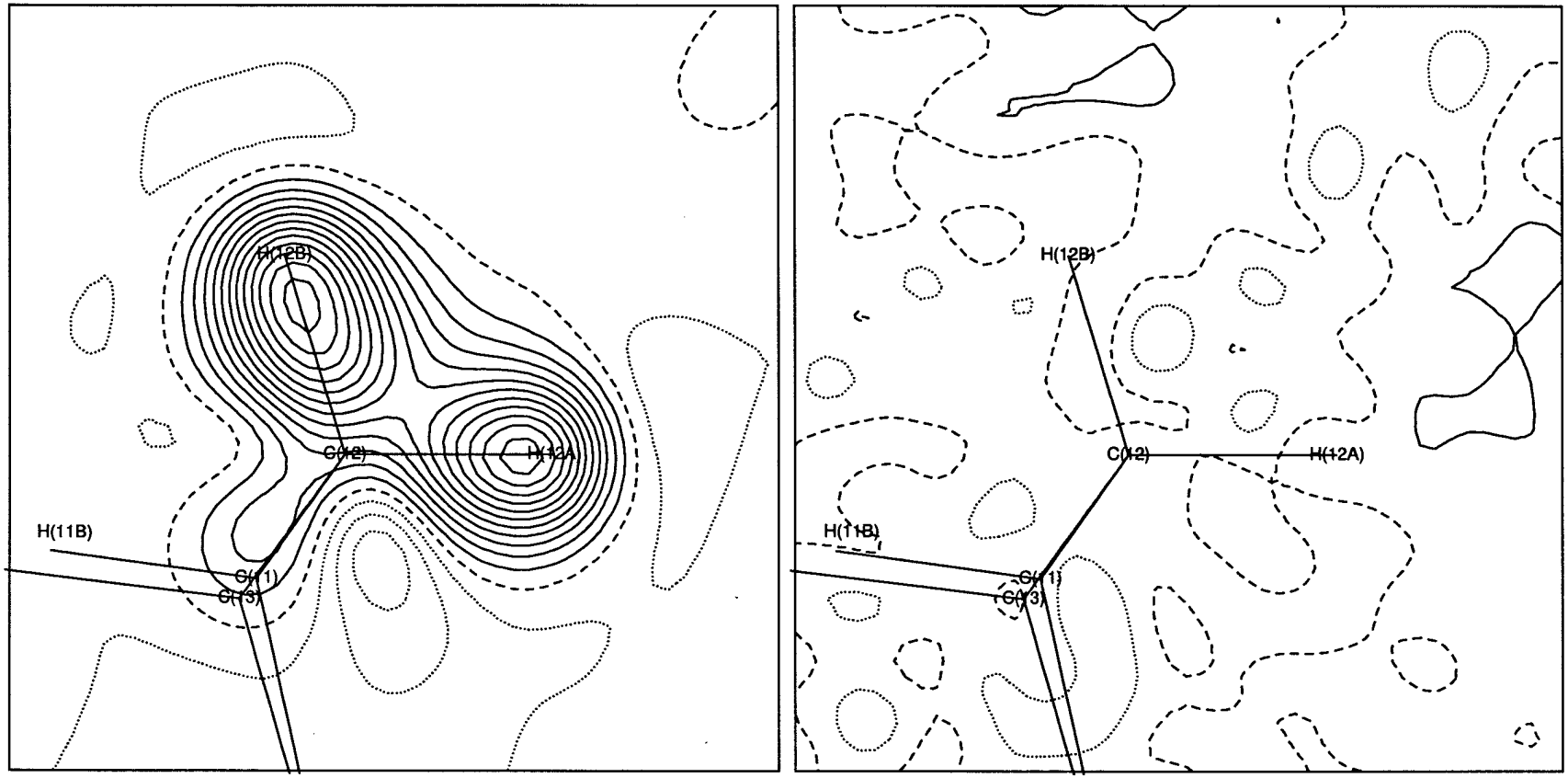

Figure D-5. Dynamic model map and residual map in the C12 – H12A – H12B plane of 17*a*-estradiol•½H_2O. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

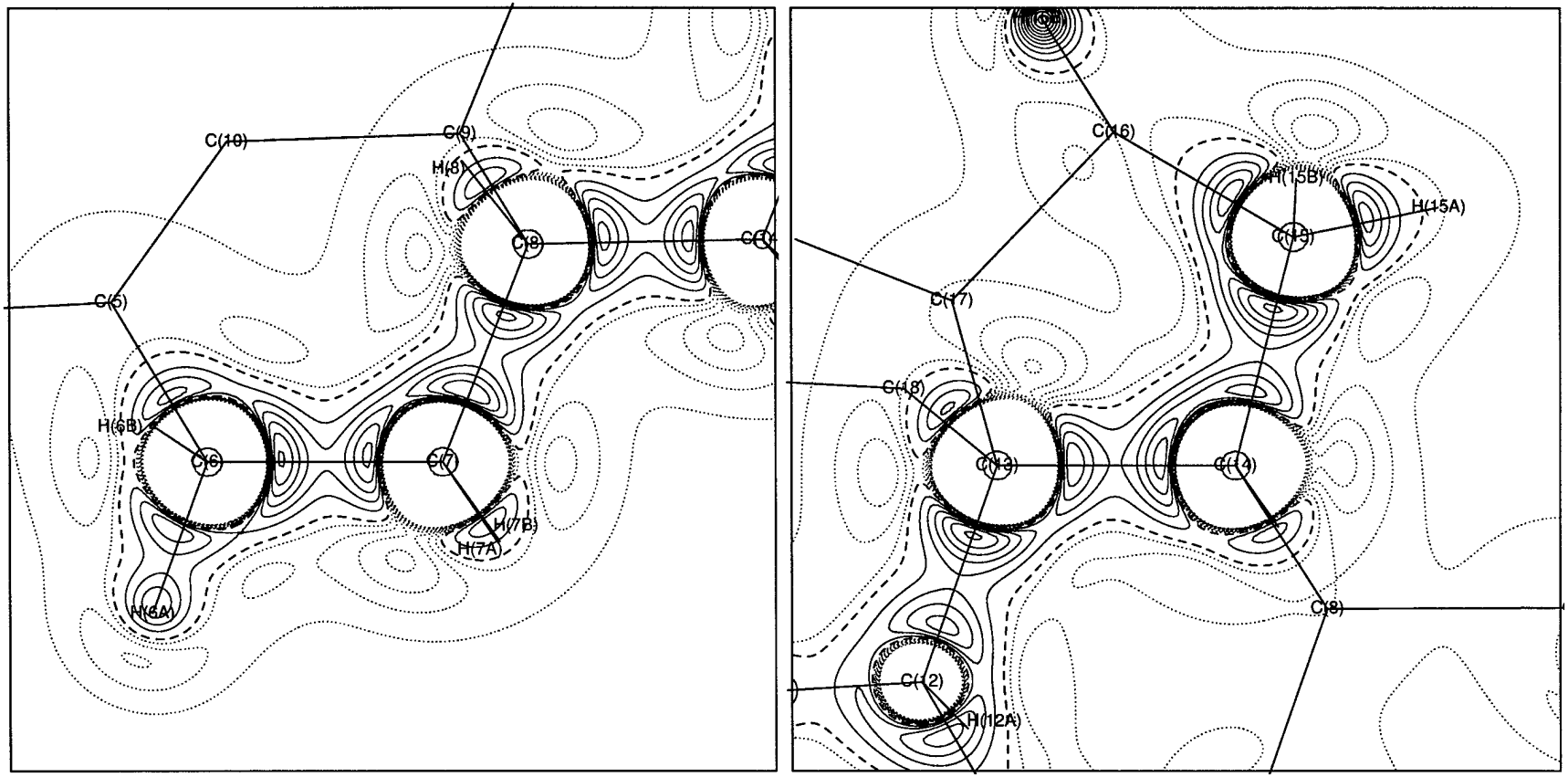

Figure D-6. The Laplacian of the total electron density of atoms at rest in the C6 – C7 – C8 and C13 – C14 – C15 planes of 17*a*-estradiol•½H_2O. Contour intervals are 5 eÅ^{-5} starting at 5 eÅ^{-5} (solid blue lines), -2 eÅ^{-5} starting at -2 eÅ^{-5} (dotted red lines), and the dashed line equals 0 eÅ^{-5}.

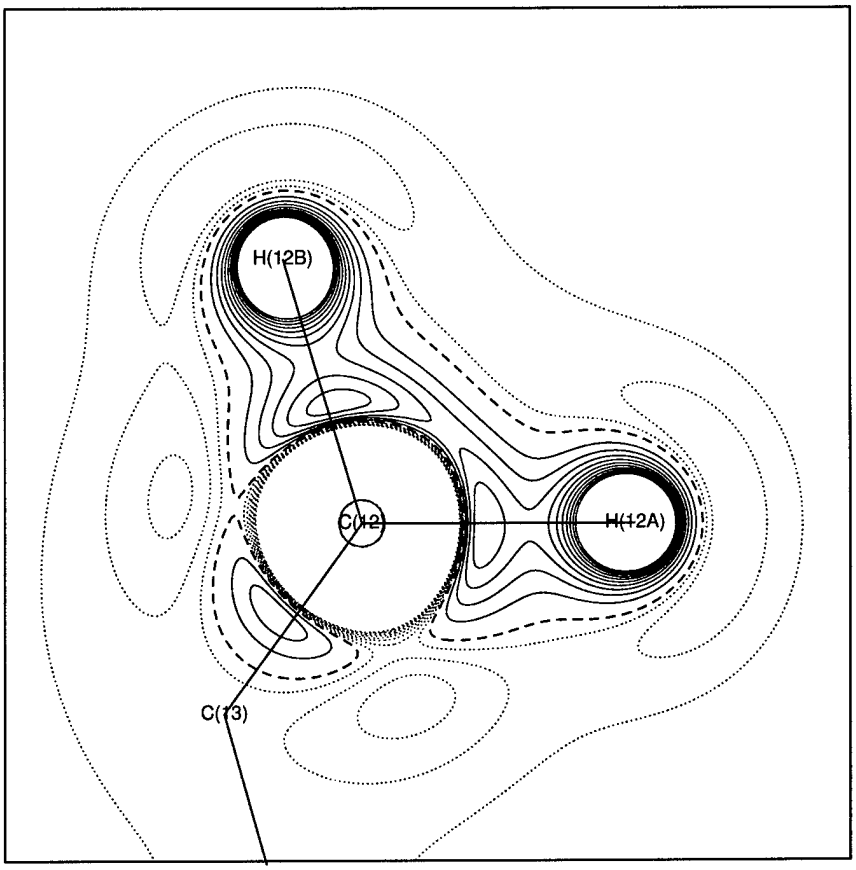

Figure D-7. The Laplacian of the total electron density of atoms at rest in the H12A – C12 – H12B plane of 17*a*-estradiol•½H_2O. Contour intervals are 5 eÅ^{-5} starting at 5 eÅ^{-5} (solid blue lines), -2 eÅ^{-5} starting at -2 eÅ^{-5} (dotted red lines), and the dashed line plots 0 eÅ^{-5}.

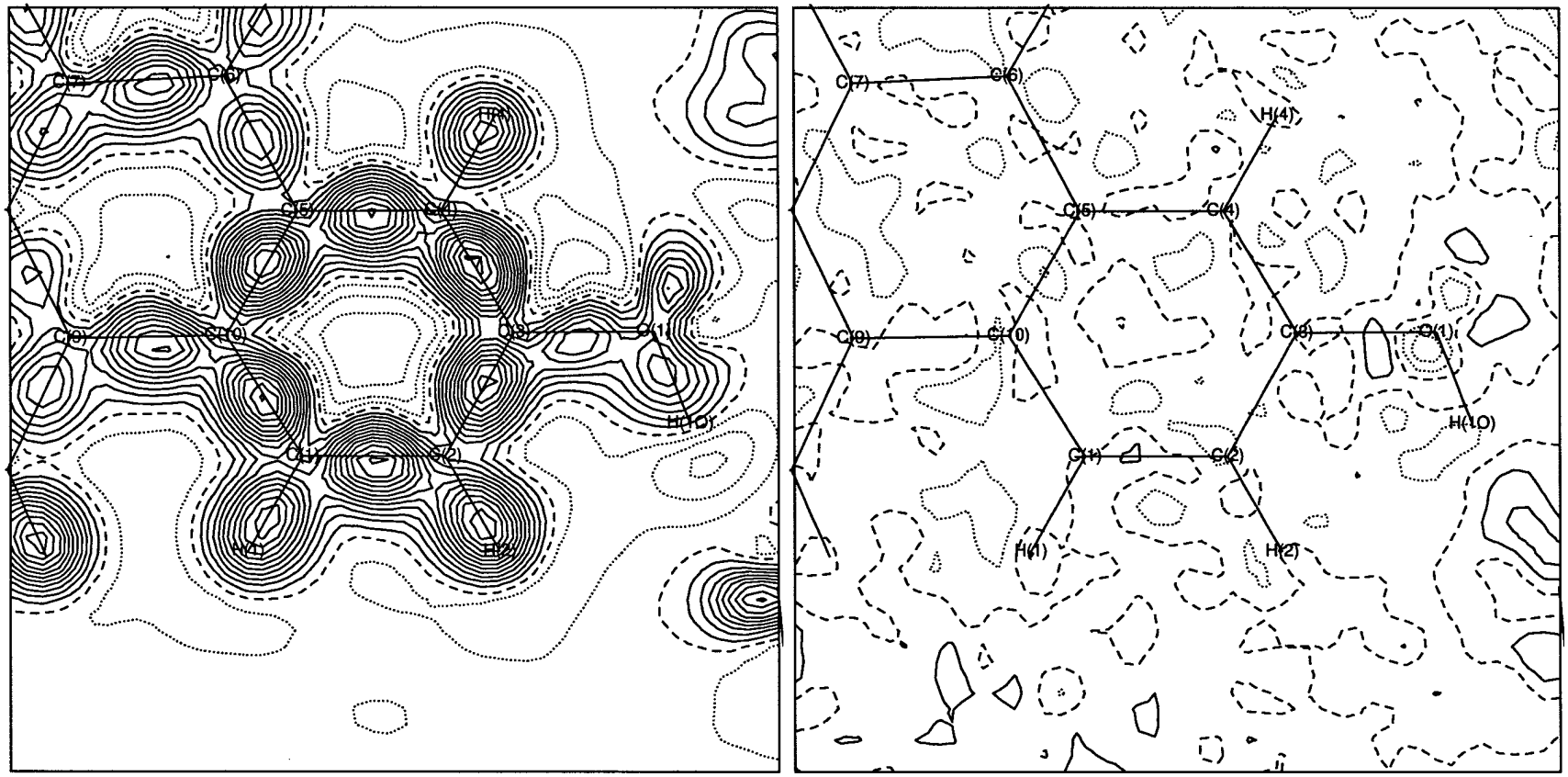

Figure D-8. Dynamic model map and residual map in the plane of the aromatic ring of 17*a*-estradiol•½H_2O. Contour intervals are 0.05 eÅ^{-3} with solid lines positive, dashed lines zero, and dotted lines negative.

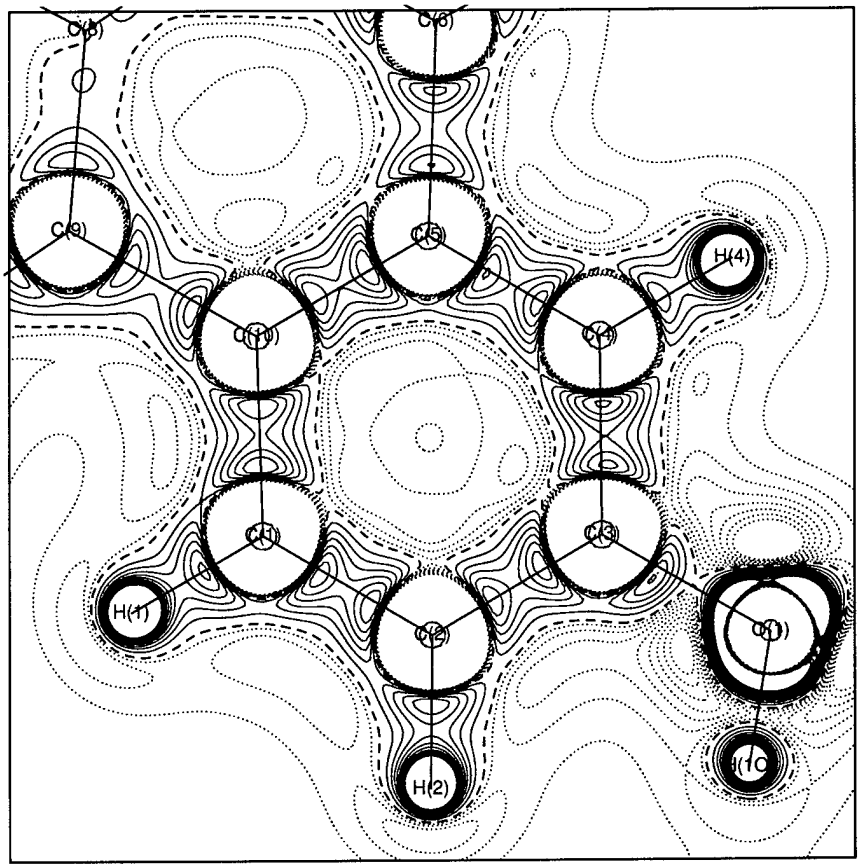

Figure D-9. The Laplacian of the total electron density of atoms at rest in the plane of the aromatic ring of 17*a*-estradiol•½H_2O. Contour intervals are 5 eÅ^{-5} starting at 5 eÅ^{-5} (solid blue lines), -2 eÅ^{-5} starting at -2 eÅ^{-5} (dotted red lines), and the dashed line plots 0 eÅ^{-5}.

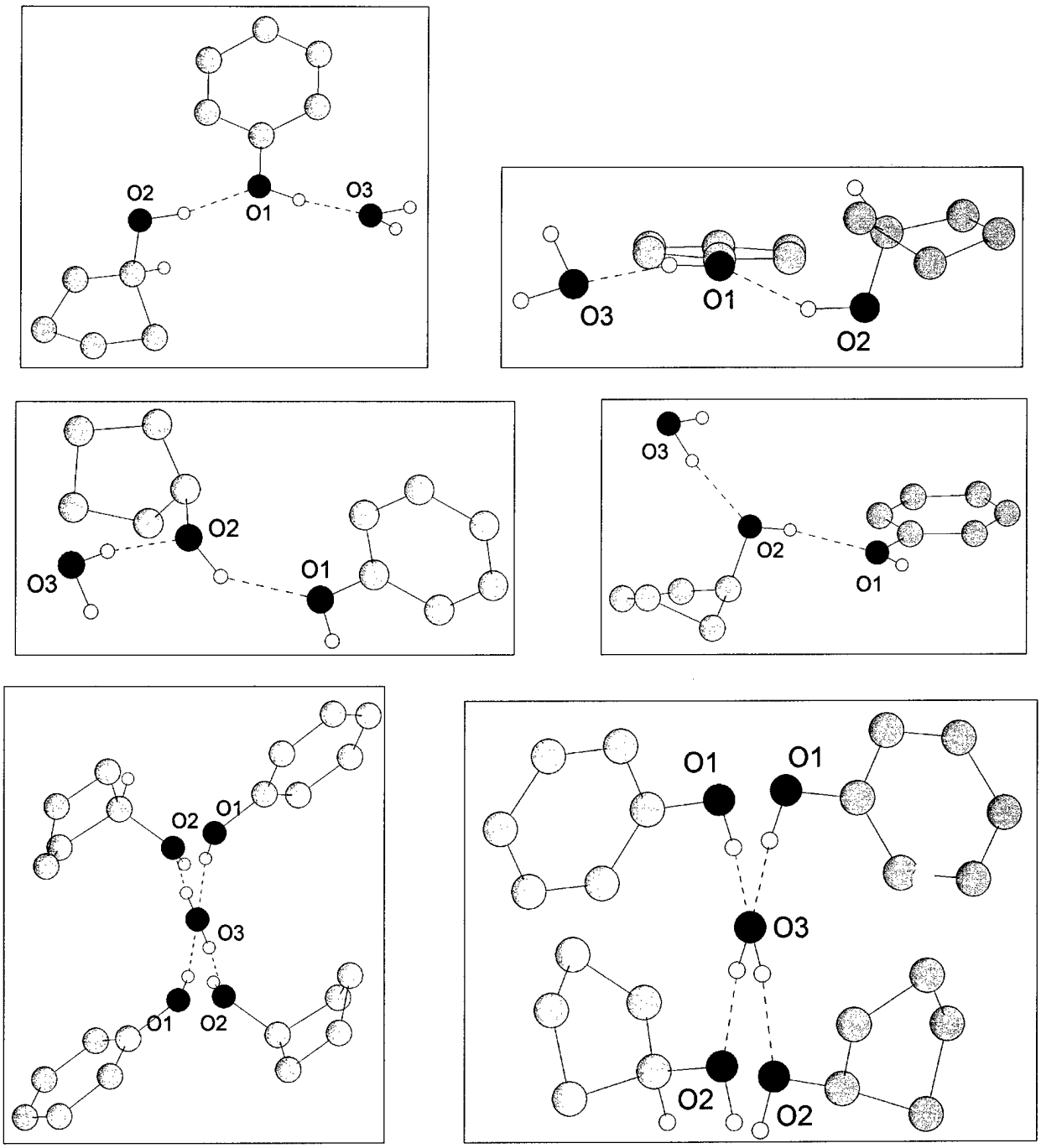

Figure D-10. Geometry of hydrogen bonding interactions of 17*a*-estradiol•½H_2O.